

MICROCELL HYBRID CLONES

	C8 and others from group c										N2 and others from group n						Y-68	Z-15
	B-5	B-24	D-1	D-2	D-8	D-14	E-21	I-23	L-34	M-16	T	T-9	W-23					
S207	X	X	X	X	●	●	●	●	X	X	X	X	X	X				
S177	X	X	X	X	●	●	●	●	●	X	X	●	X	X				
VPOLYMORPHIC	●	●	X	X	●	●	●	●	●	X	●	X	●	X				
AND GENETIC	●	●	●	●	●	●	●	●	●	●	●	●	●					
MARKERS	●	●	X	X	●	●	●	●	●	X	●	X	●	X				
S156	X	X	X	X	●	●	●	●	●	X	X	X	X	X				
S159	X	X	X	X	●	●	●	●	●	X	X	X	X	X				
CHROMOSOME	I	I	I	I	I	I	I	I	I	I	T	T	I	I	I			

I: INDEPENDENT T: TRANSLOCATED

FIG. 1

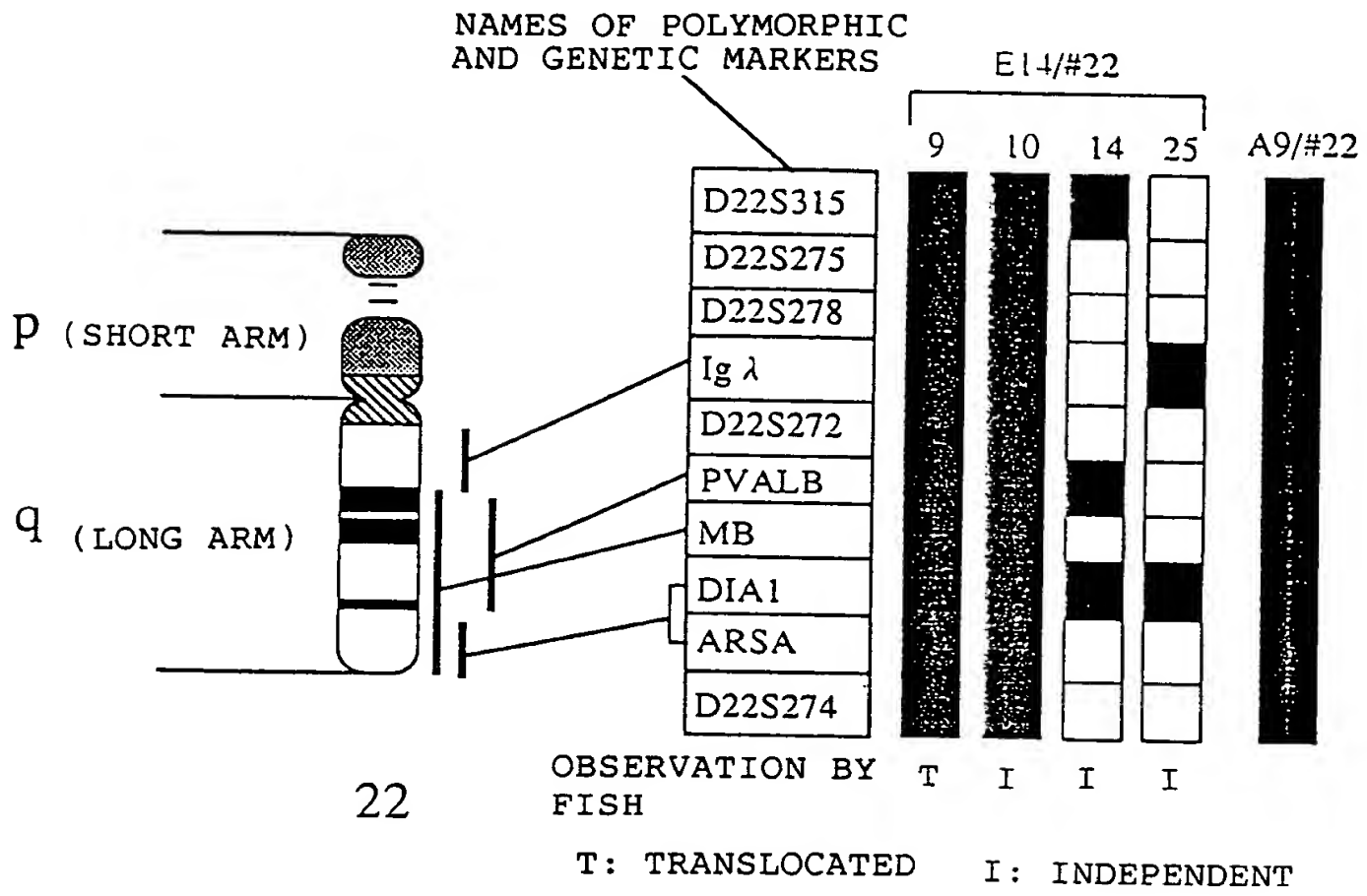


FIG. 2

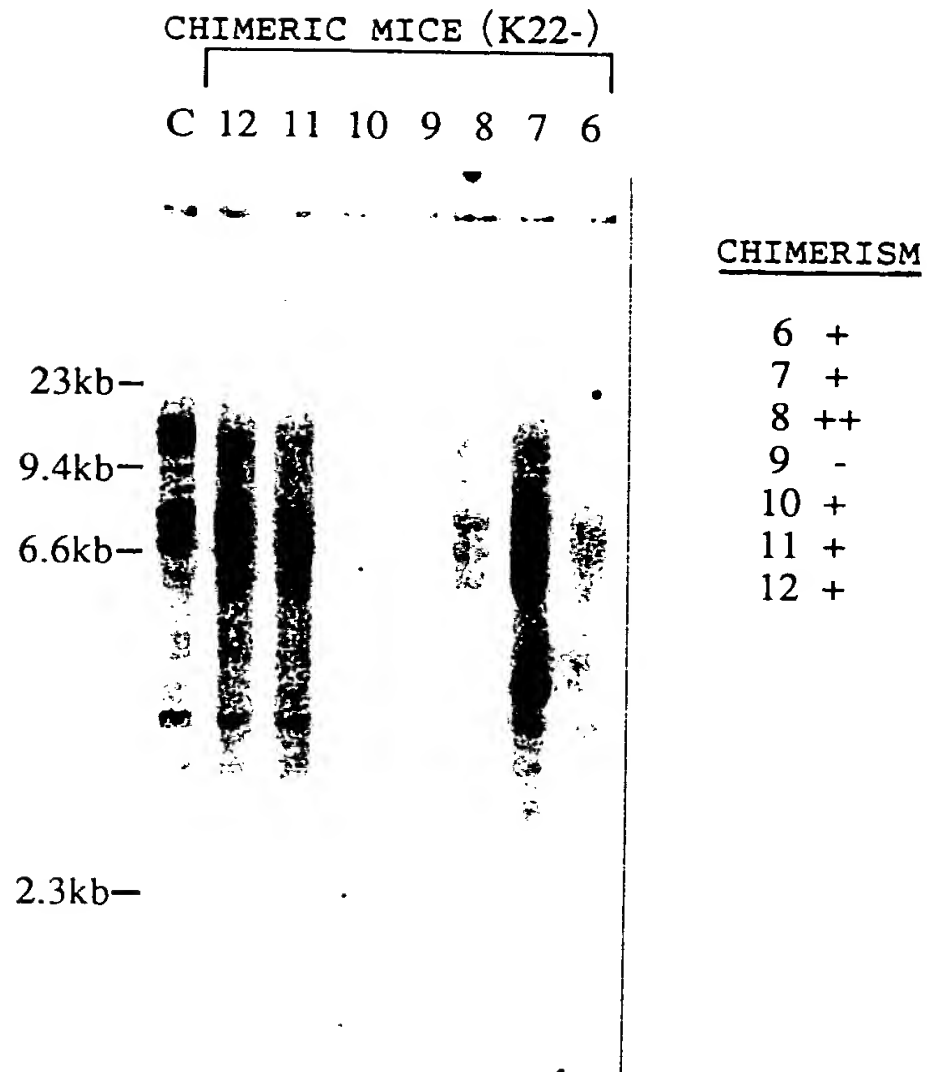
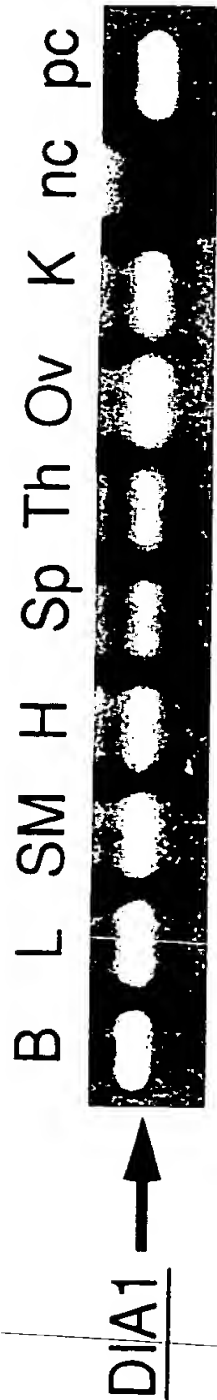


FIG. 3

B : BRAIN
L : LIVER
SM : SKELETAL MUSCLE
H : HEART
Sp : SPLEEN
Th : THYMUS
Ov : OVARY
K : KIDNEY
nc : NEGATIVE CONTROL
pc : POSITIVE CONTROL



DIA1 : HUMAN CYTOCHROME b5 REDUCTASE

FIG. 4

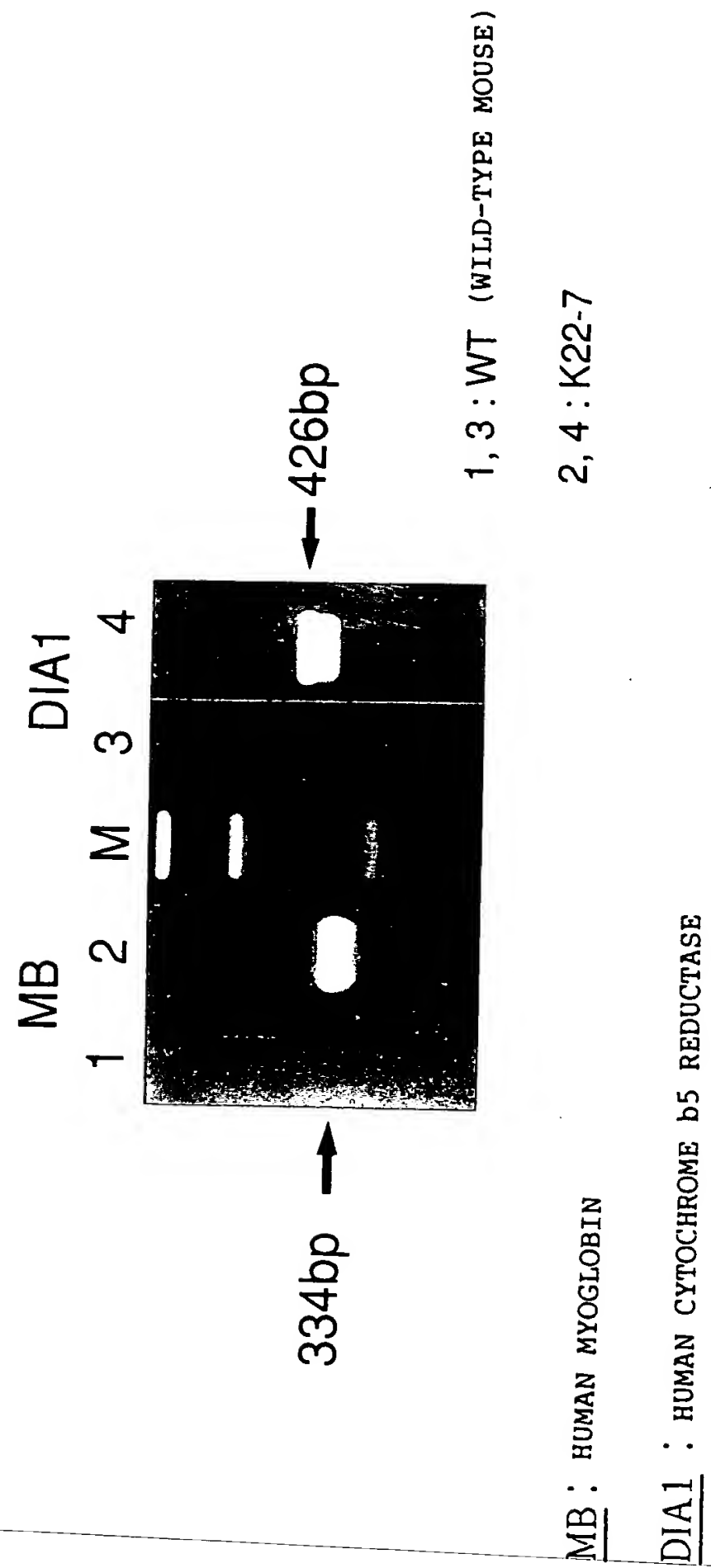


FIG. 5

B : BRAIN
H : HEART
Th : THYMUS
L : LIVER
Sp : SPLEEN
K : KIDNEY
Ov : OVARY
SM : SKELETAL MUSCLE
M : MOLECULAR WEIGHT MARKER



MB : HUMAN MYOGLOBIN

DIA1 : HUMAN CYTOCHROME b5 REDUCTASE

FIG. 6

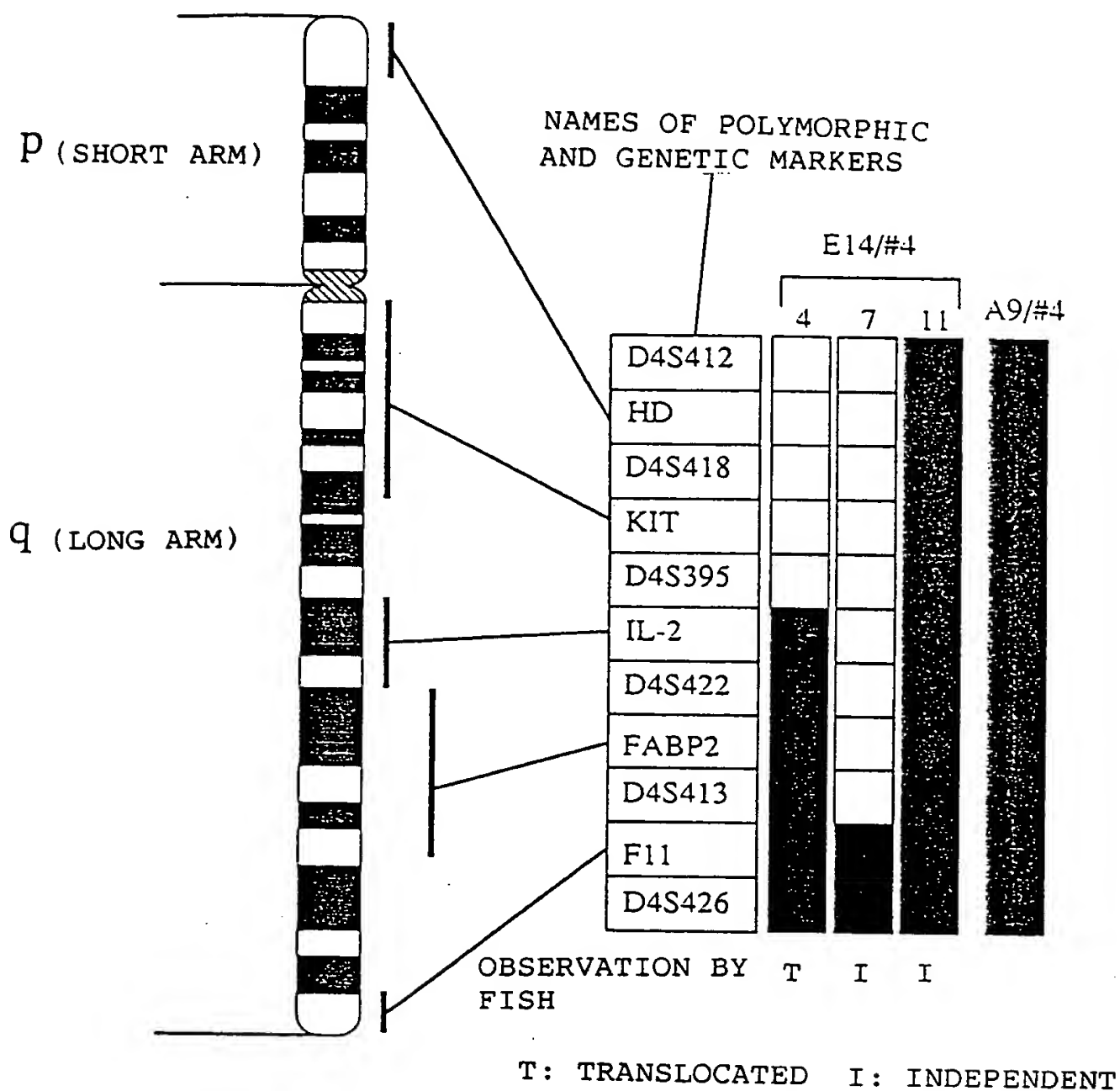


FIG. 7

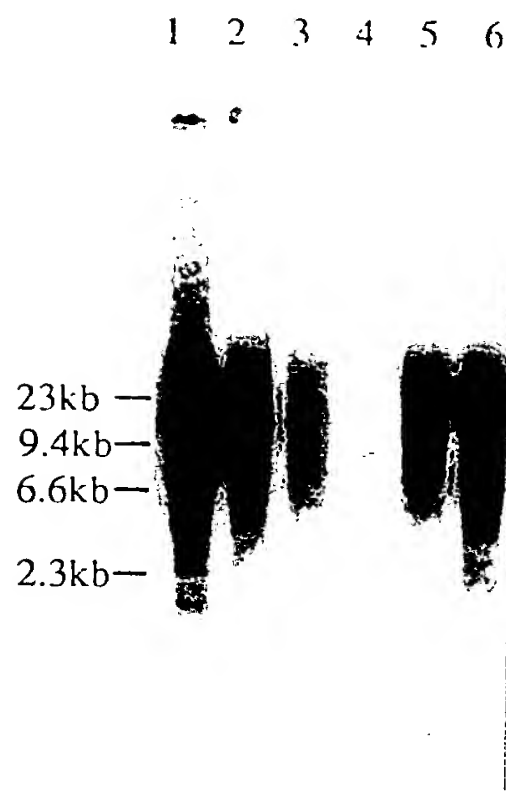


FIG. 8

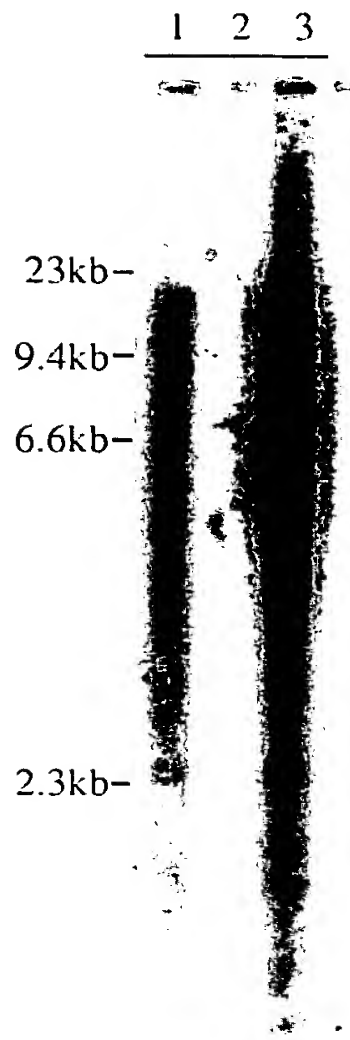


FIG. 9

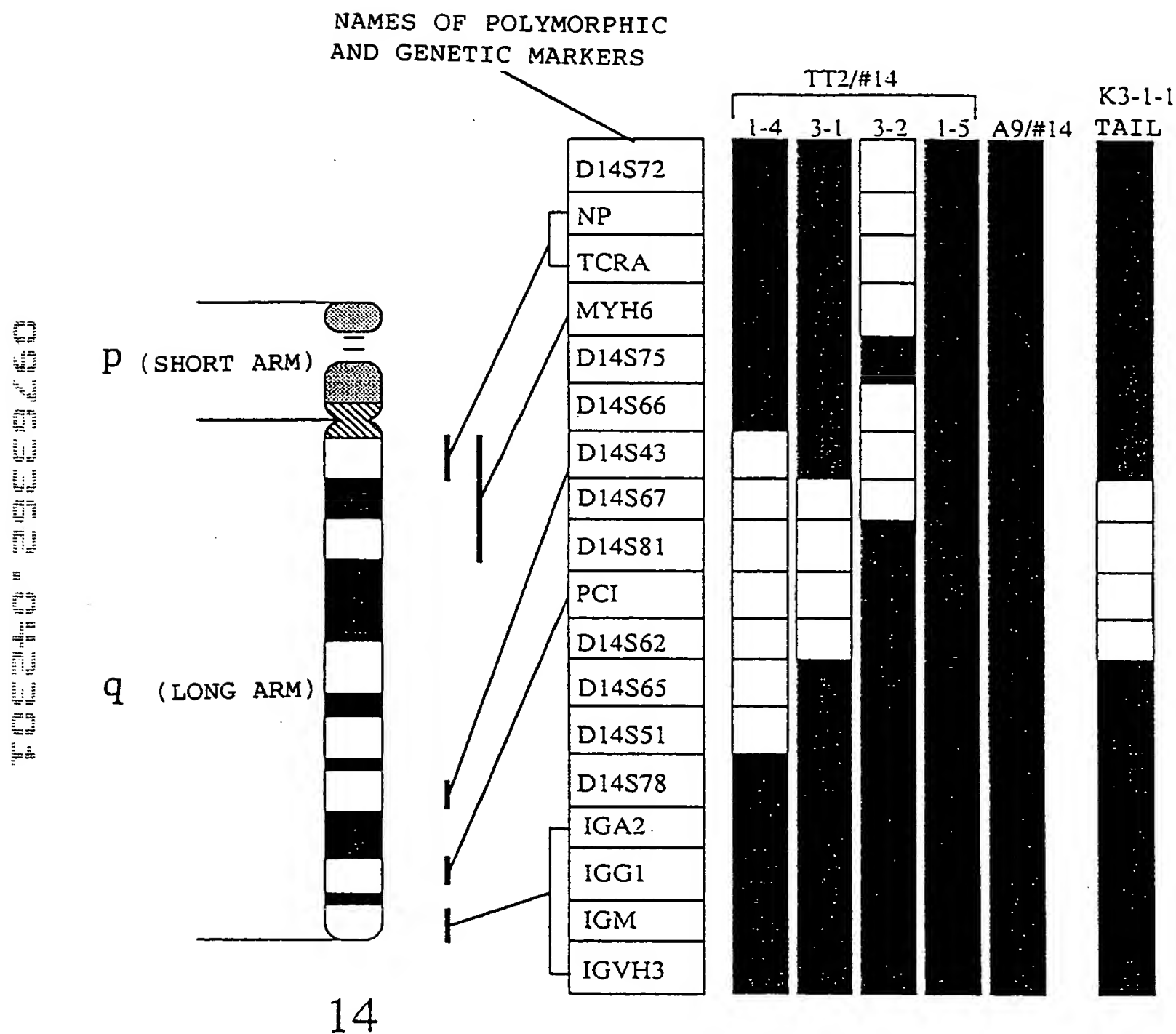
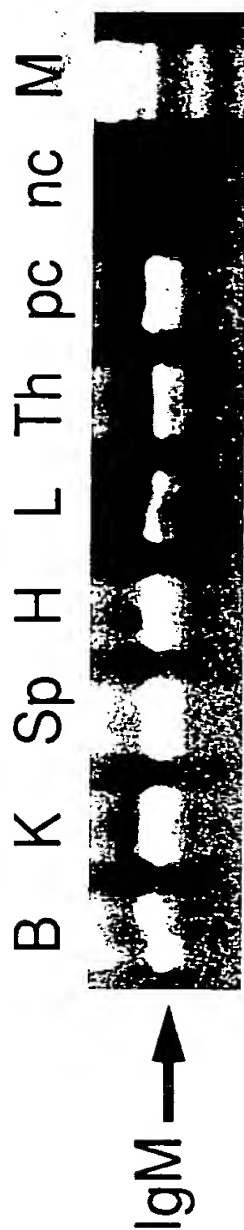


FIG. 10

B : BRAIN
K : KIDNEY
Sp : SPLEEN
H : HEART
L : LIVER
Th : THYMUS
pc : POSITIVE CONTROL
nc : NEGATIVE CONTROL
M : MOLECULAR WEIGHT MARKER



IgM : HUMAN IMMUNOGLOBULIN μ CHAIN

FIG. 11

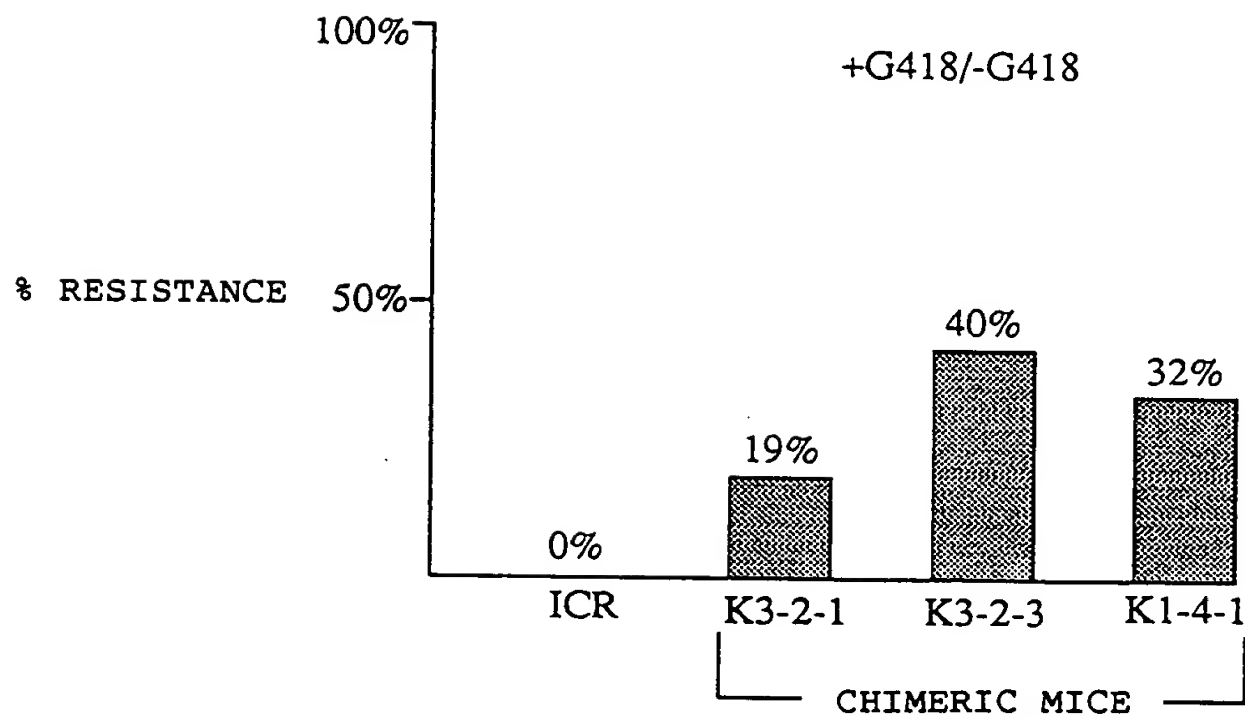


FIG. 12

FIG. 13

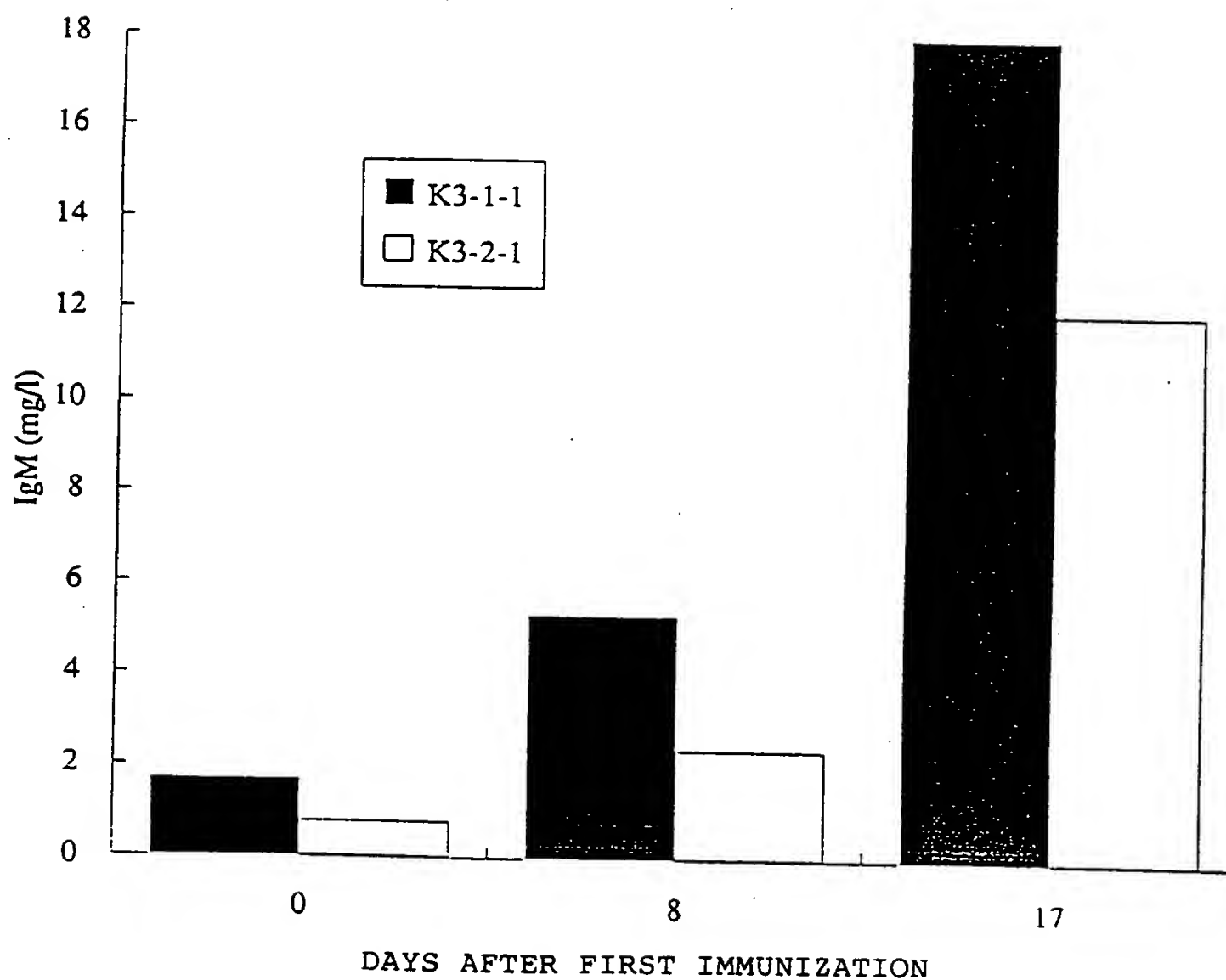


FIG. 14

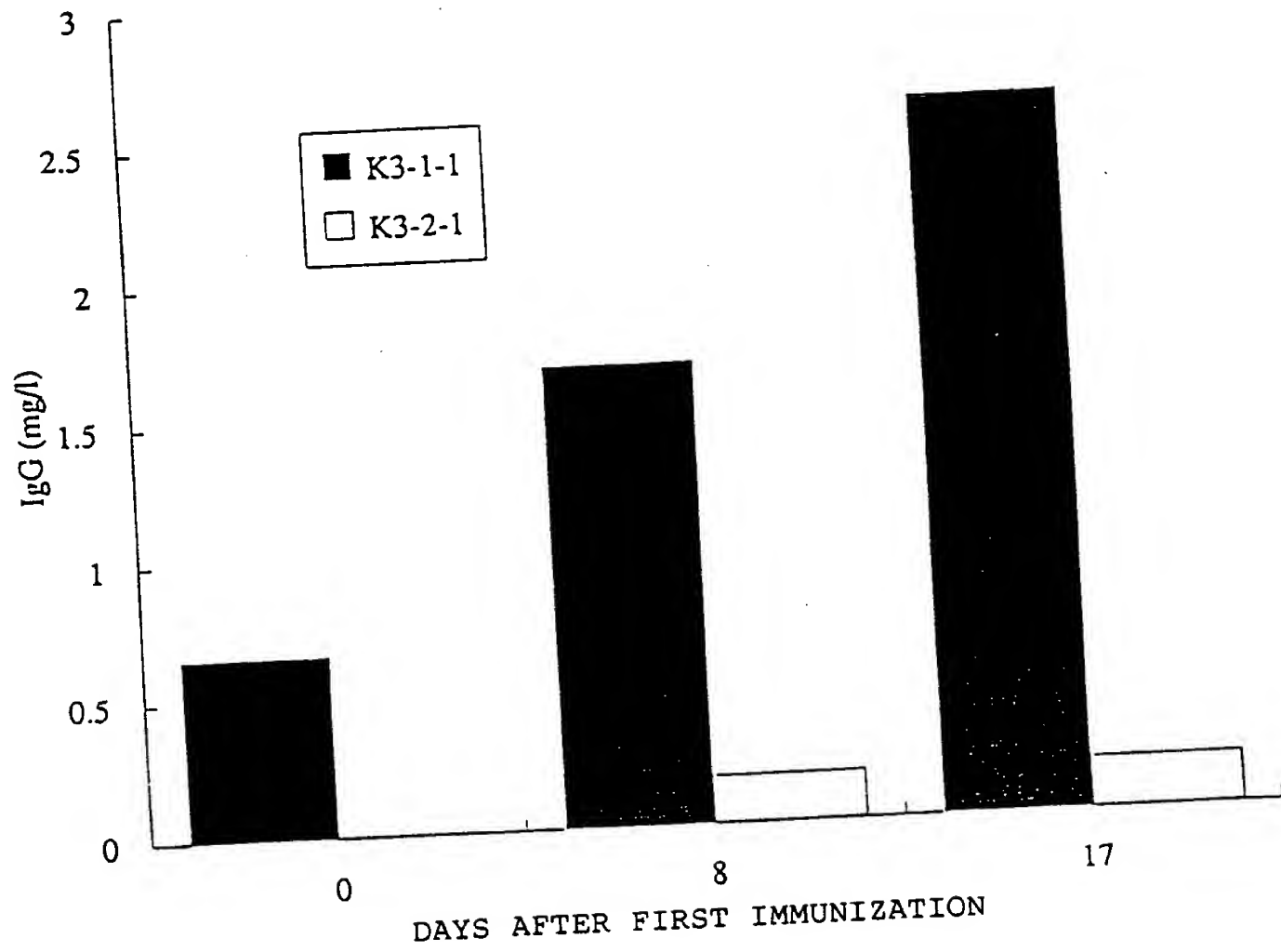
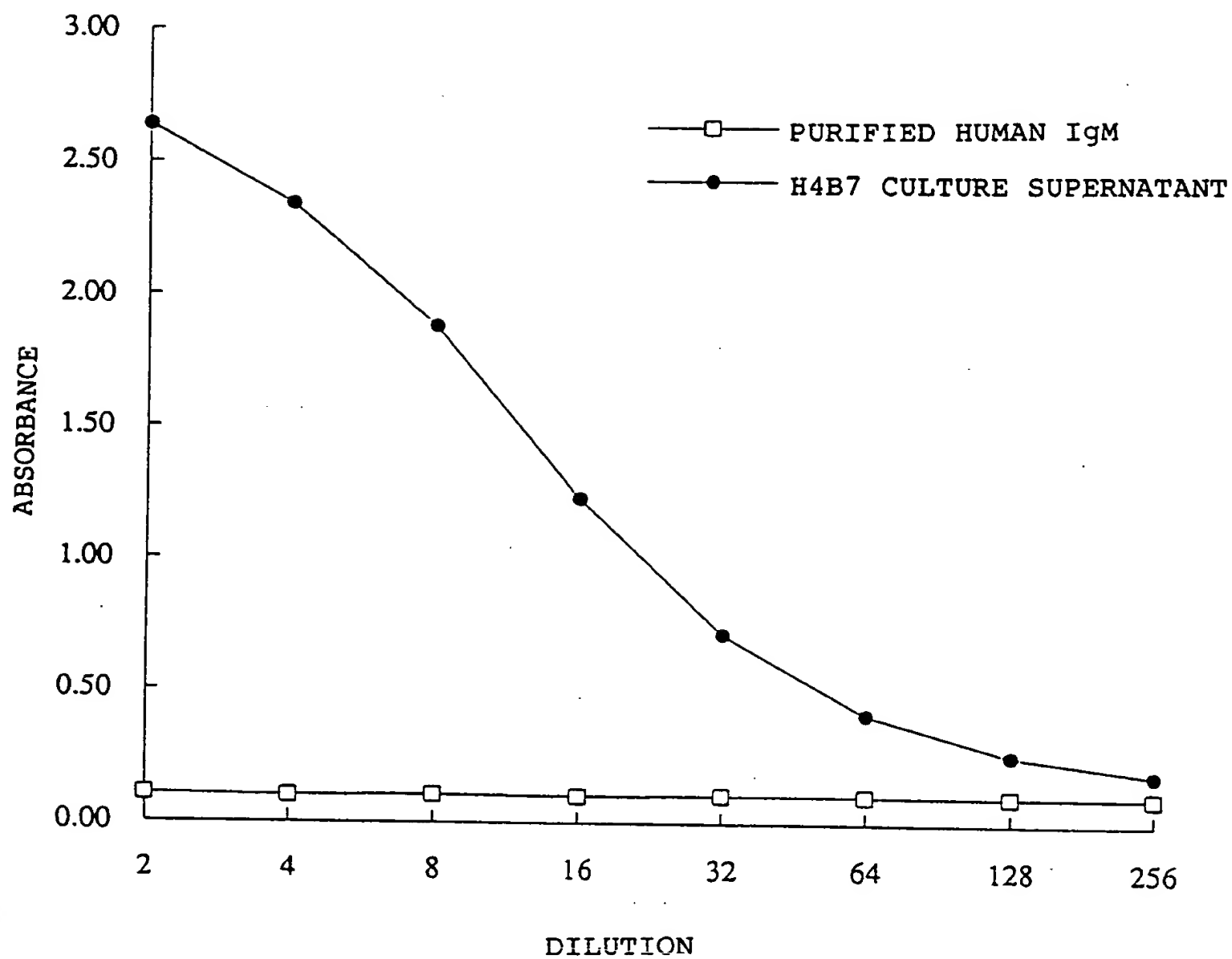


FIG. 15



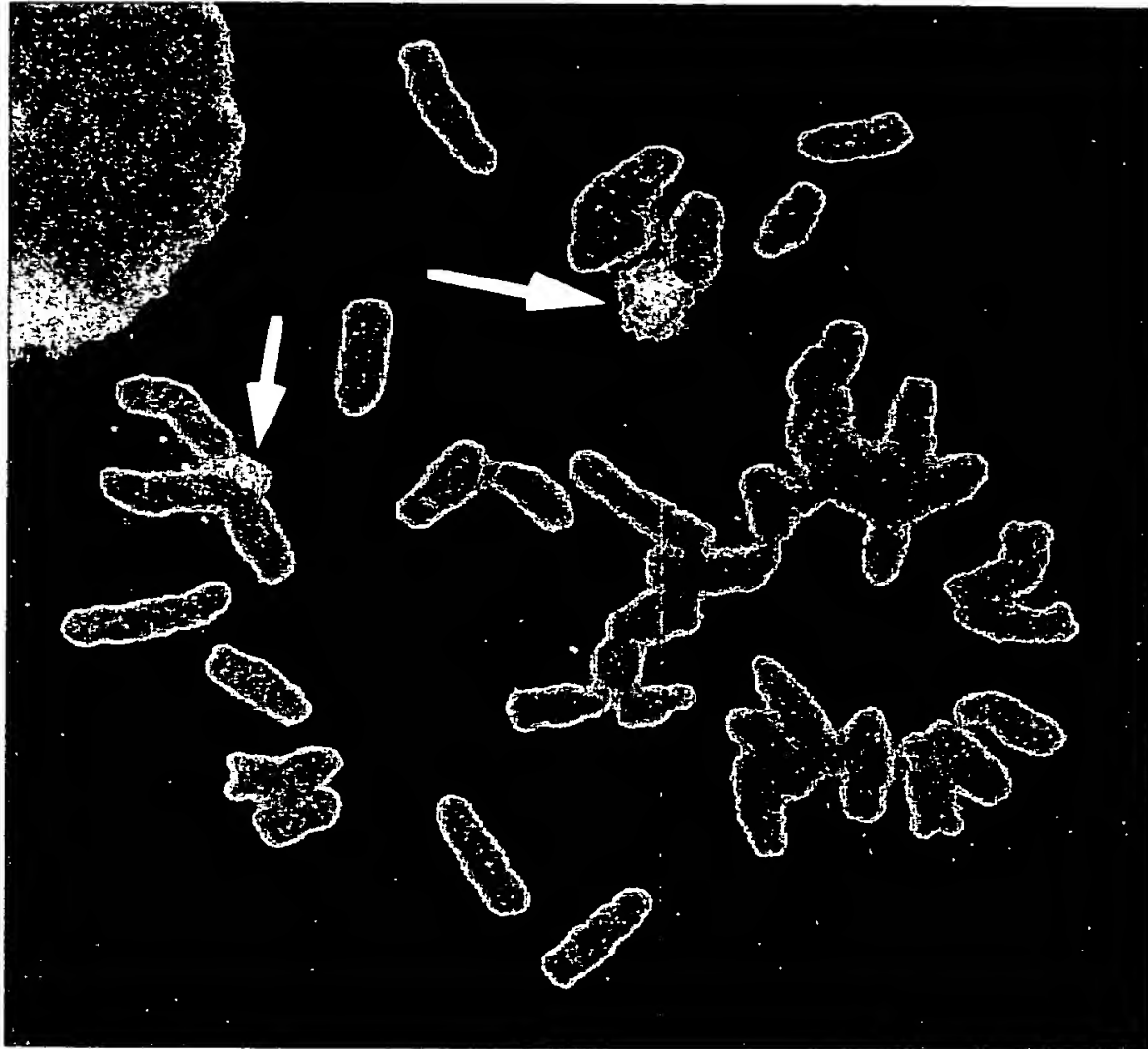


FIG. 16

FIG. 17

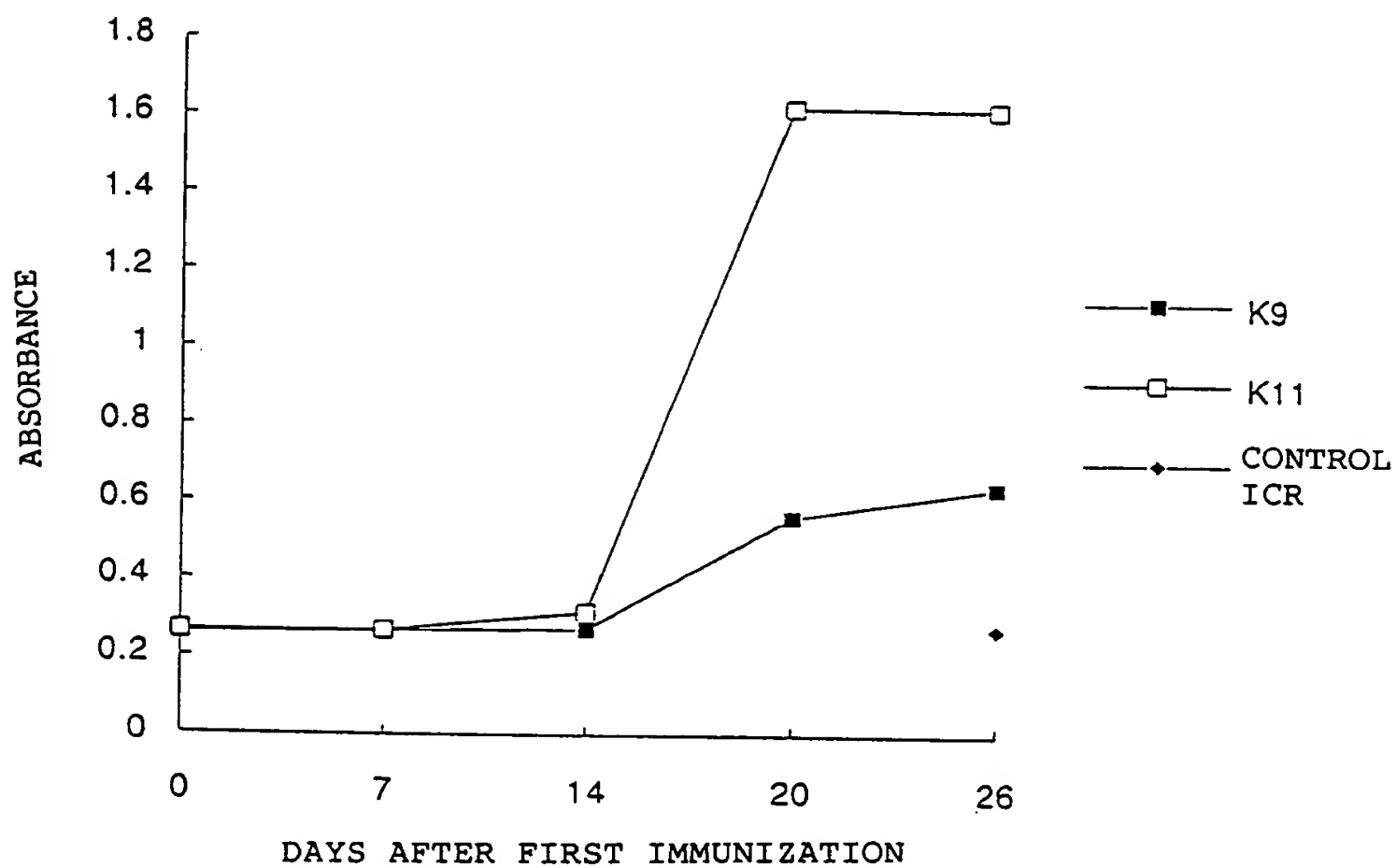


FIG. 18

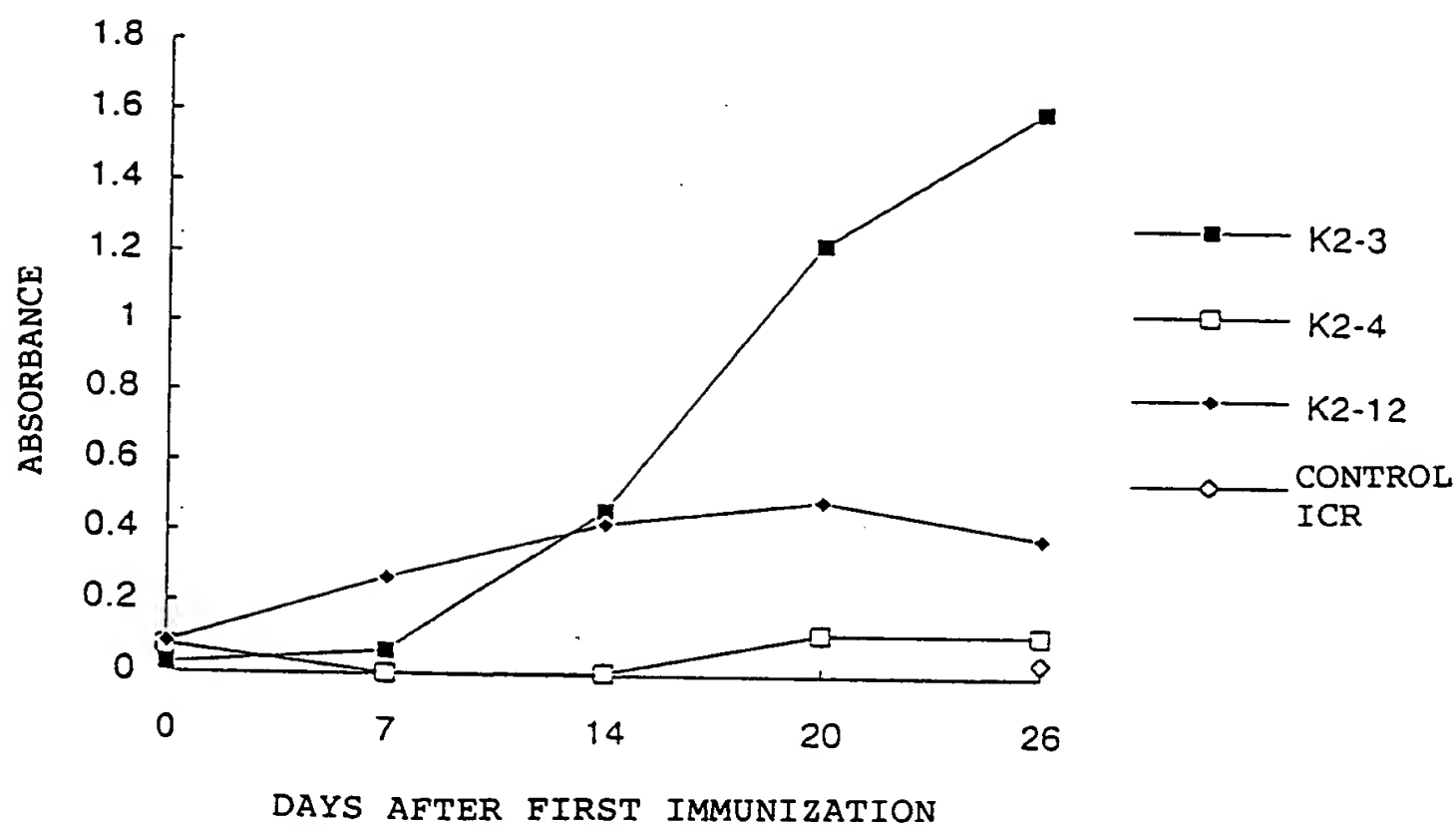


FIG. 19

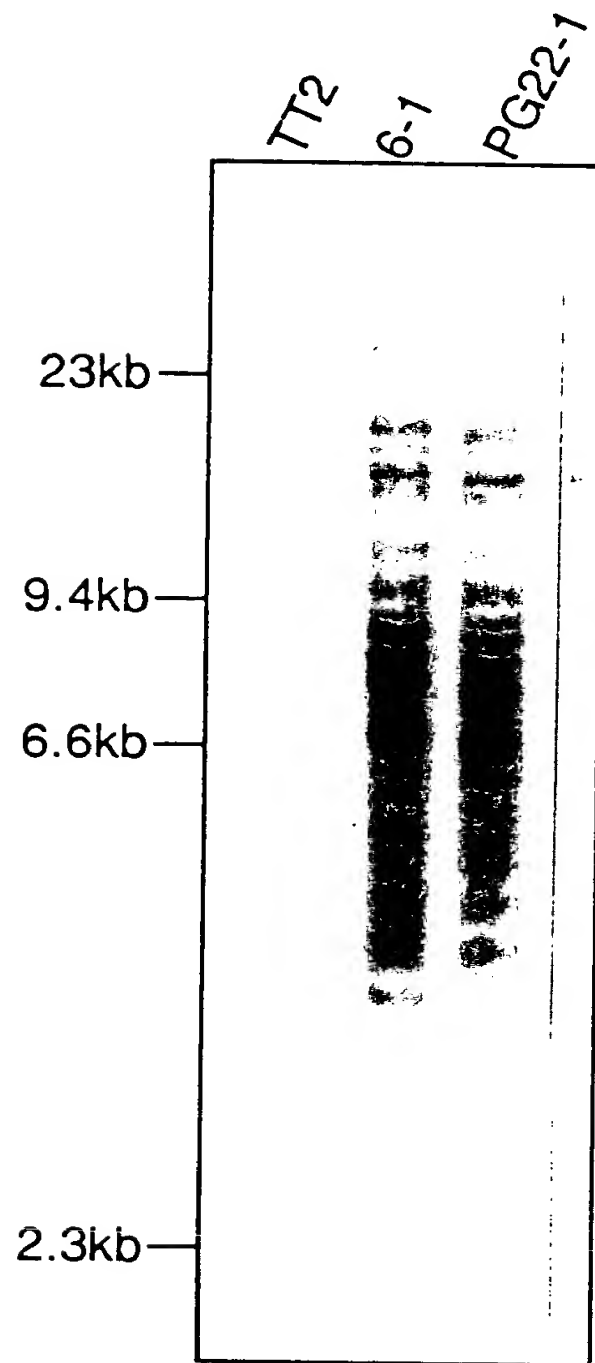


FIG. 20

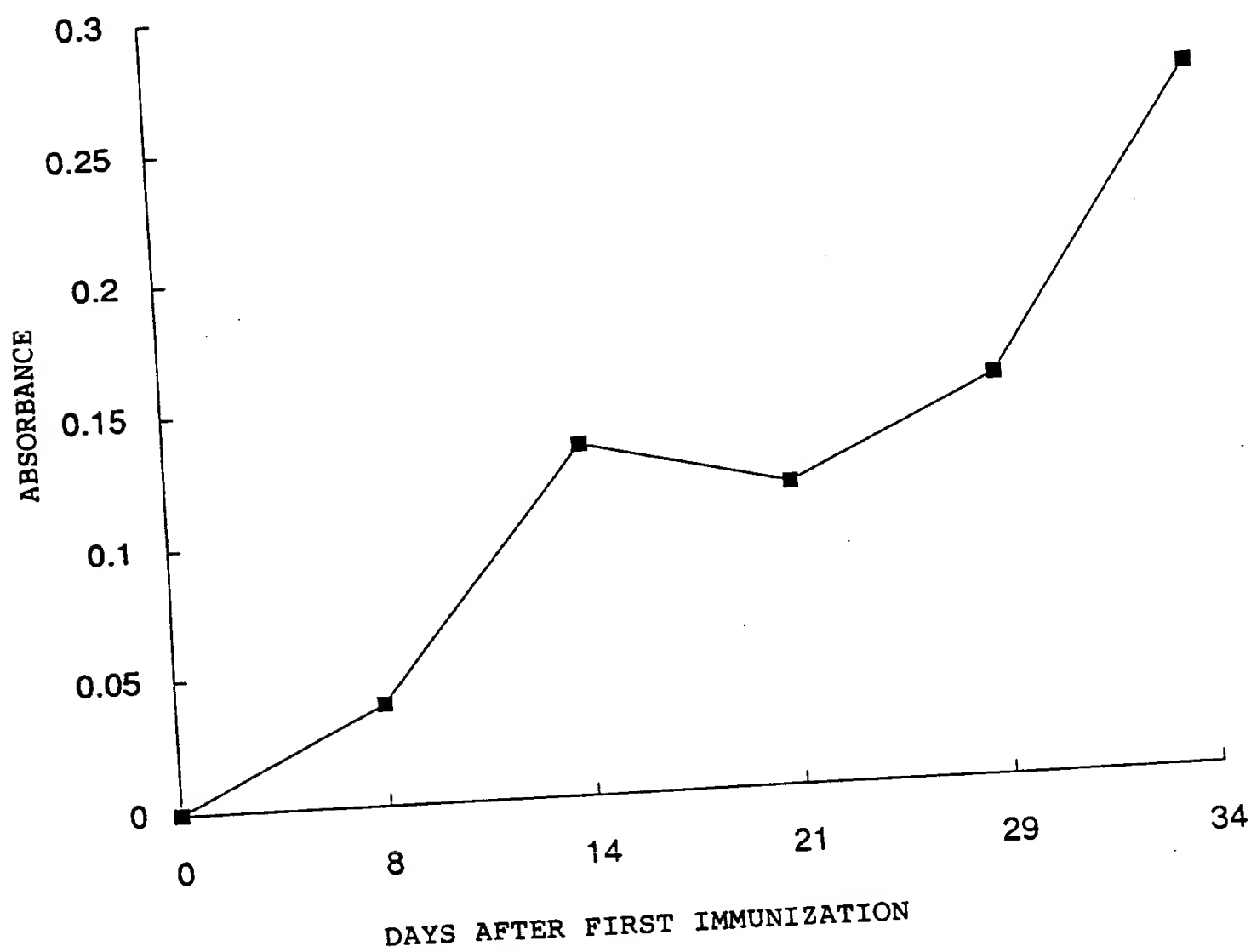
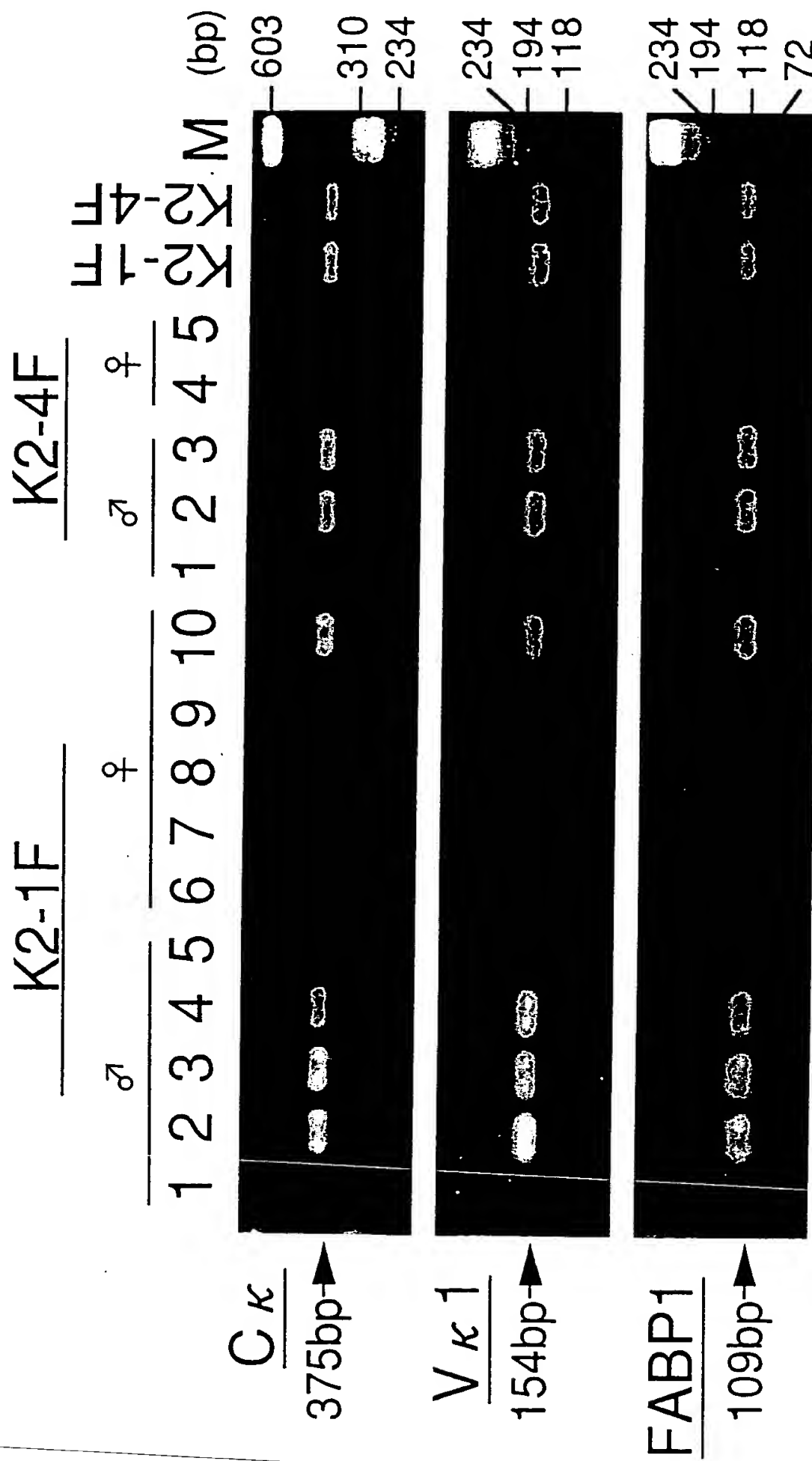


FIG. 21



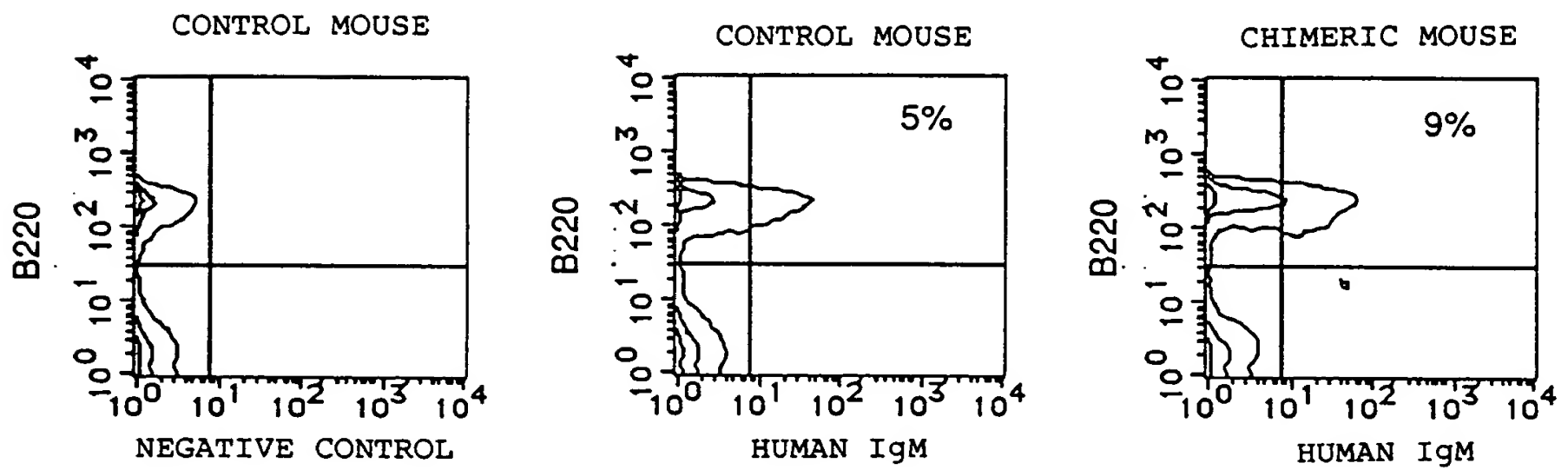


FIG. 22

FIG. 23

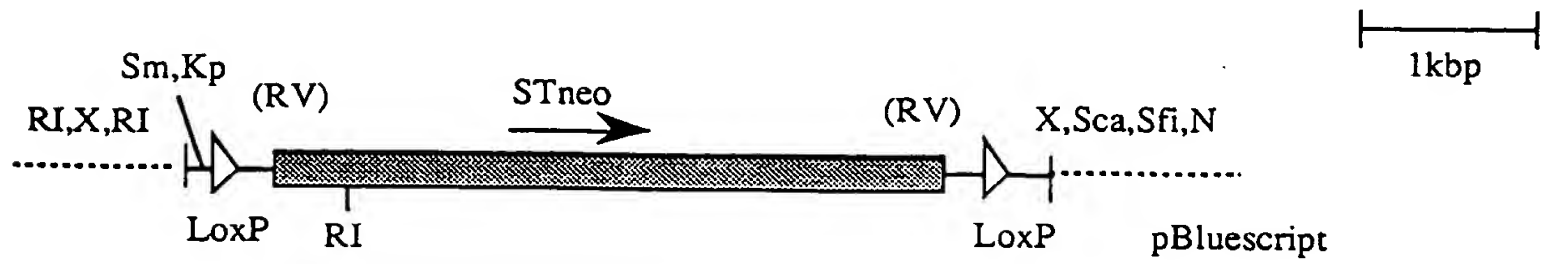


FIG. 24

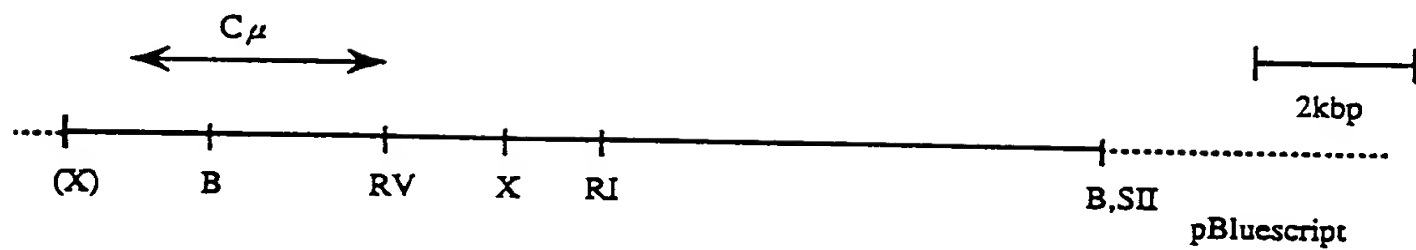


FIG. 25

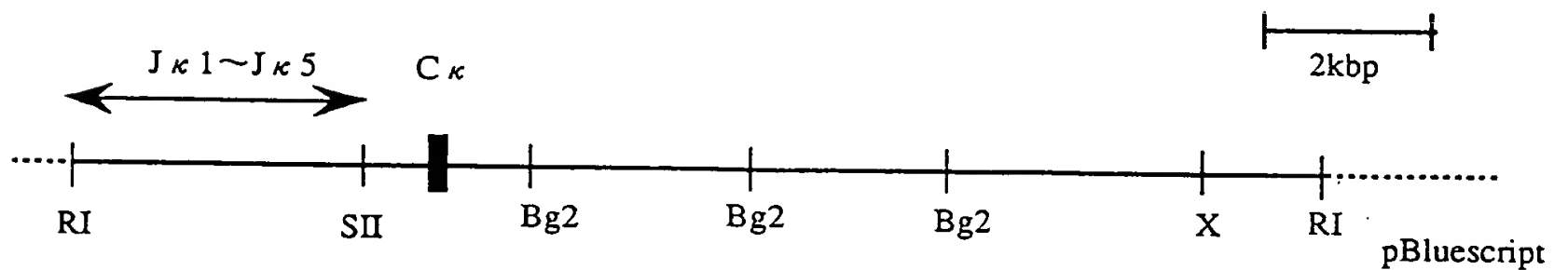


FIG. 26

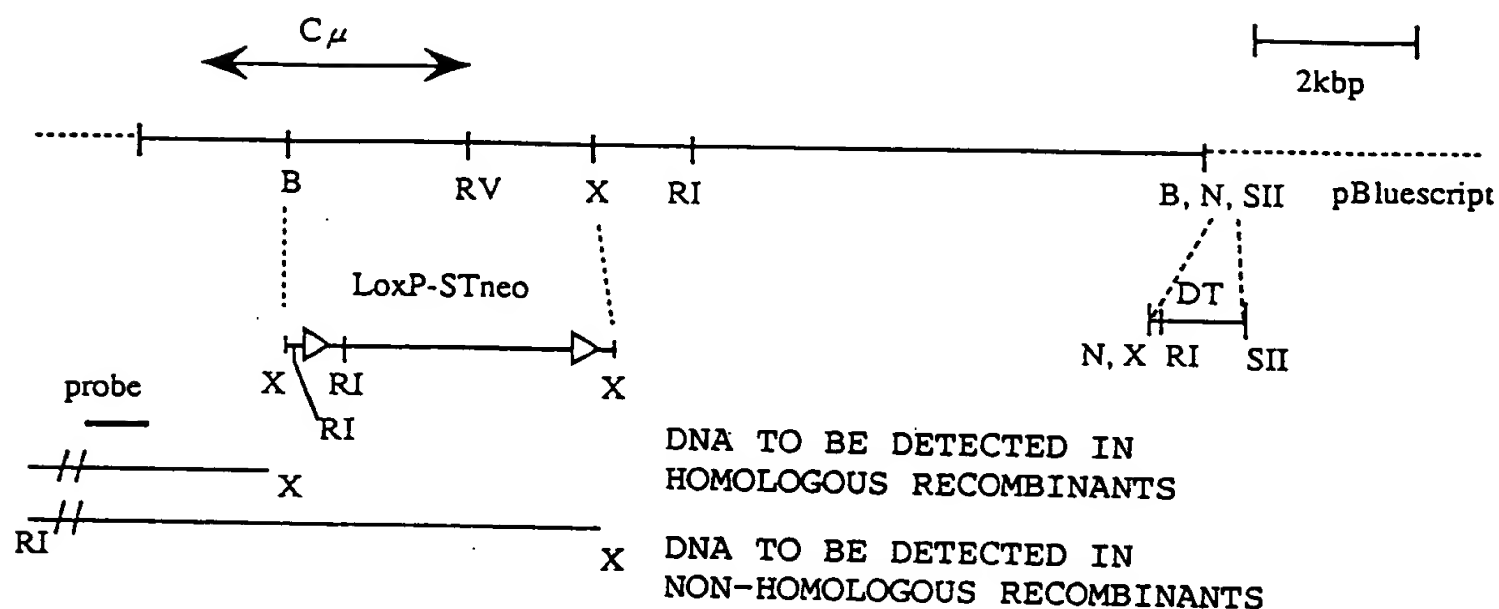


FIG. 27

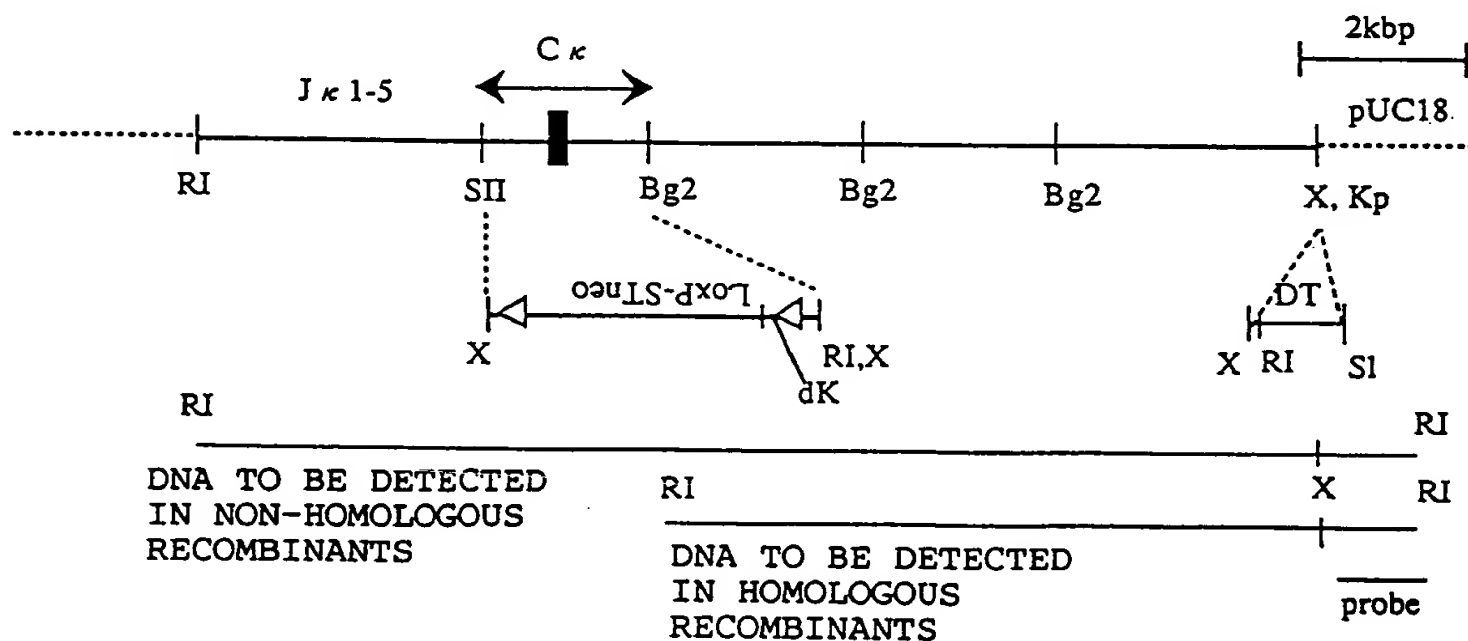


FIG. 28

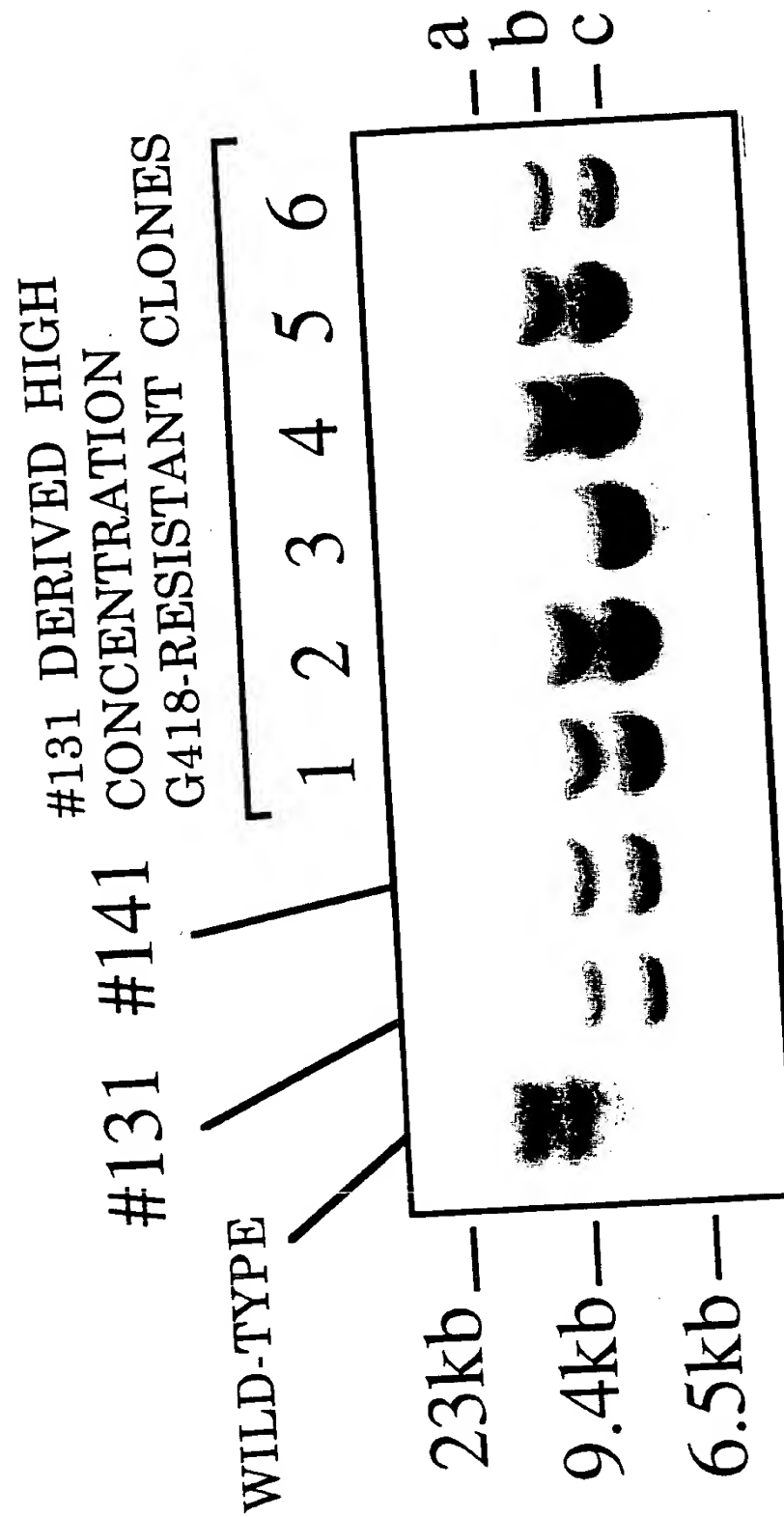


FIG. 29 TRANSFORMANT TT2F CELL CLONES

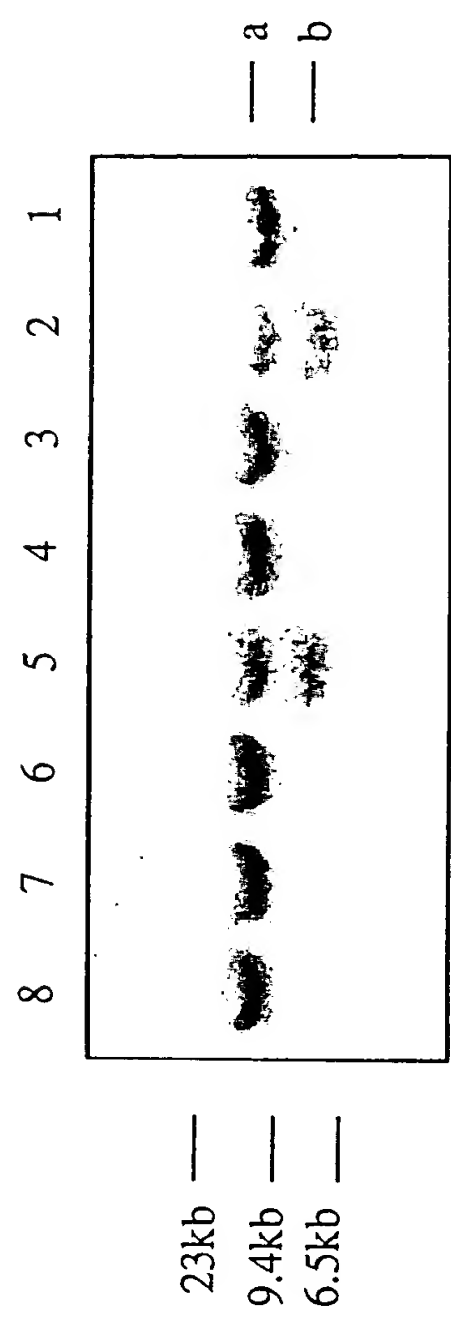


FIG. 30

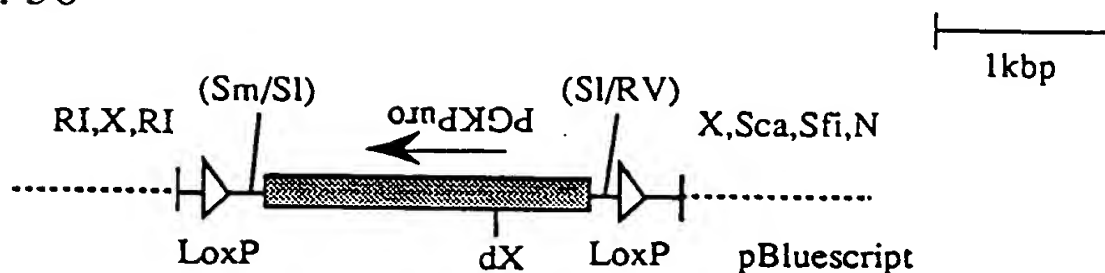
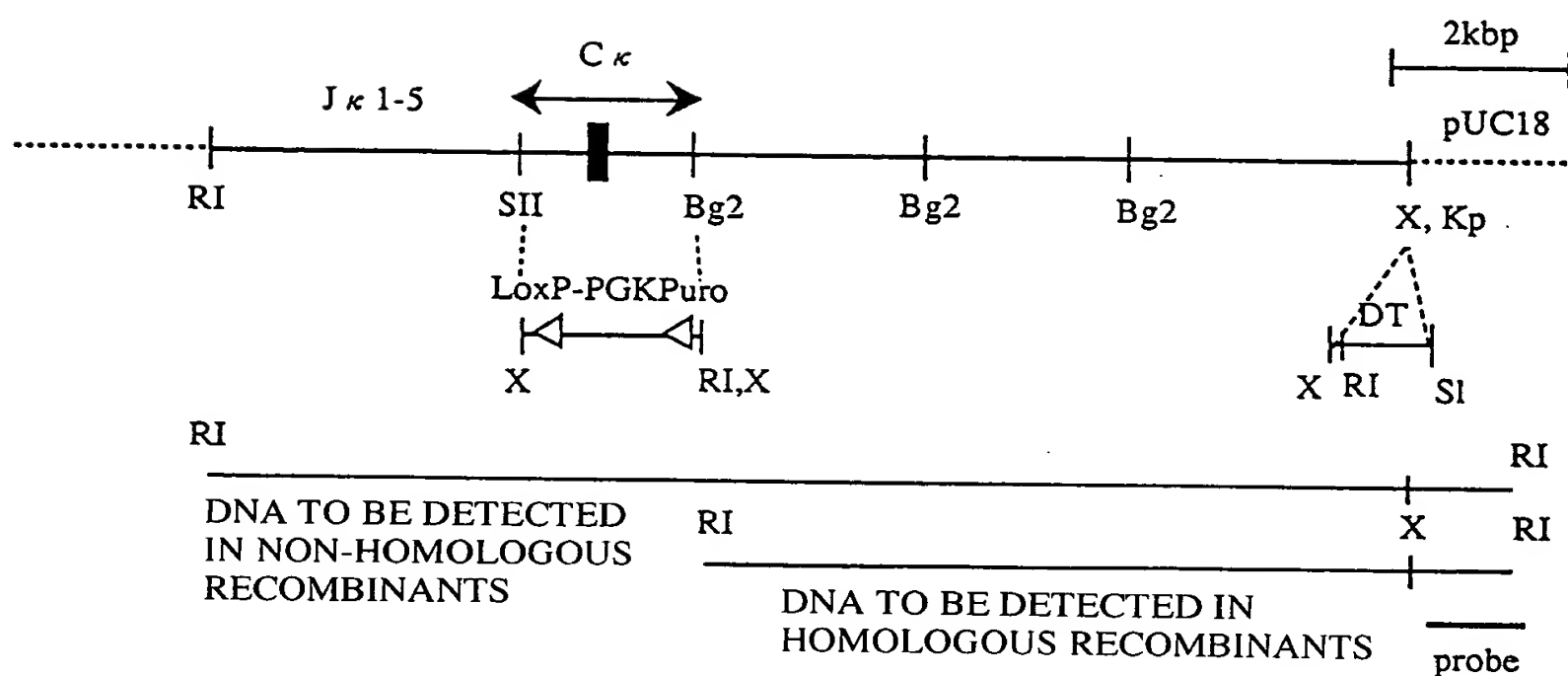


FIG. 31



RESTRICTION ENZYMES:

Kp: KpnI, B: BamHI, Bg2:Bgl2, RI: EcoRI, RV: EcoRV, N: Not, SI: SalI, Sca: ScaI, Sfi: SfiI,
Sm: Sma, X: XhoI, (X): XhoI RESTRICTION SITE FROM λ VECTOR
dK: KpnI RESTRICTION SITE DELETED, dX: XhoI RESTRICTION SITE DELETED
(Sm/SI): LIGATED TO SmaI RESTRICTION SITE AFTER SalI BLUNTING
(SI/RV): LIGATED TO EcoRV RESTRICTION SITE AFTER SalI BLUNTING
DOTTED PORTION: pBluescript SKII(+) OR pUC18 PLASMID DNA

◁▷ : LoxP SEQUENCE

FIG. 32
HIGH CONCENTRATION G418 RESISTANT TT2F CELL CLONES

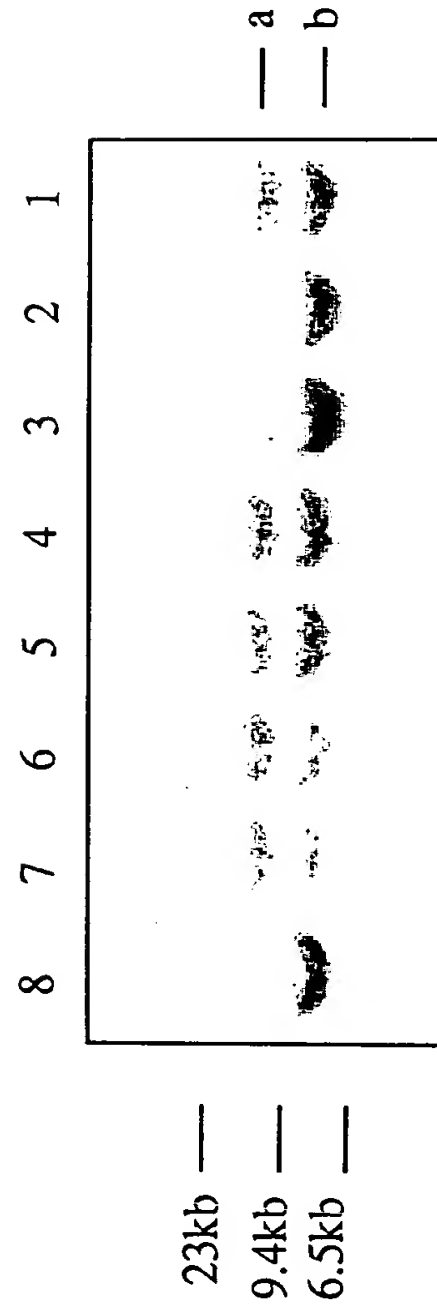
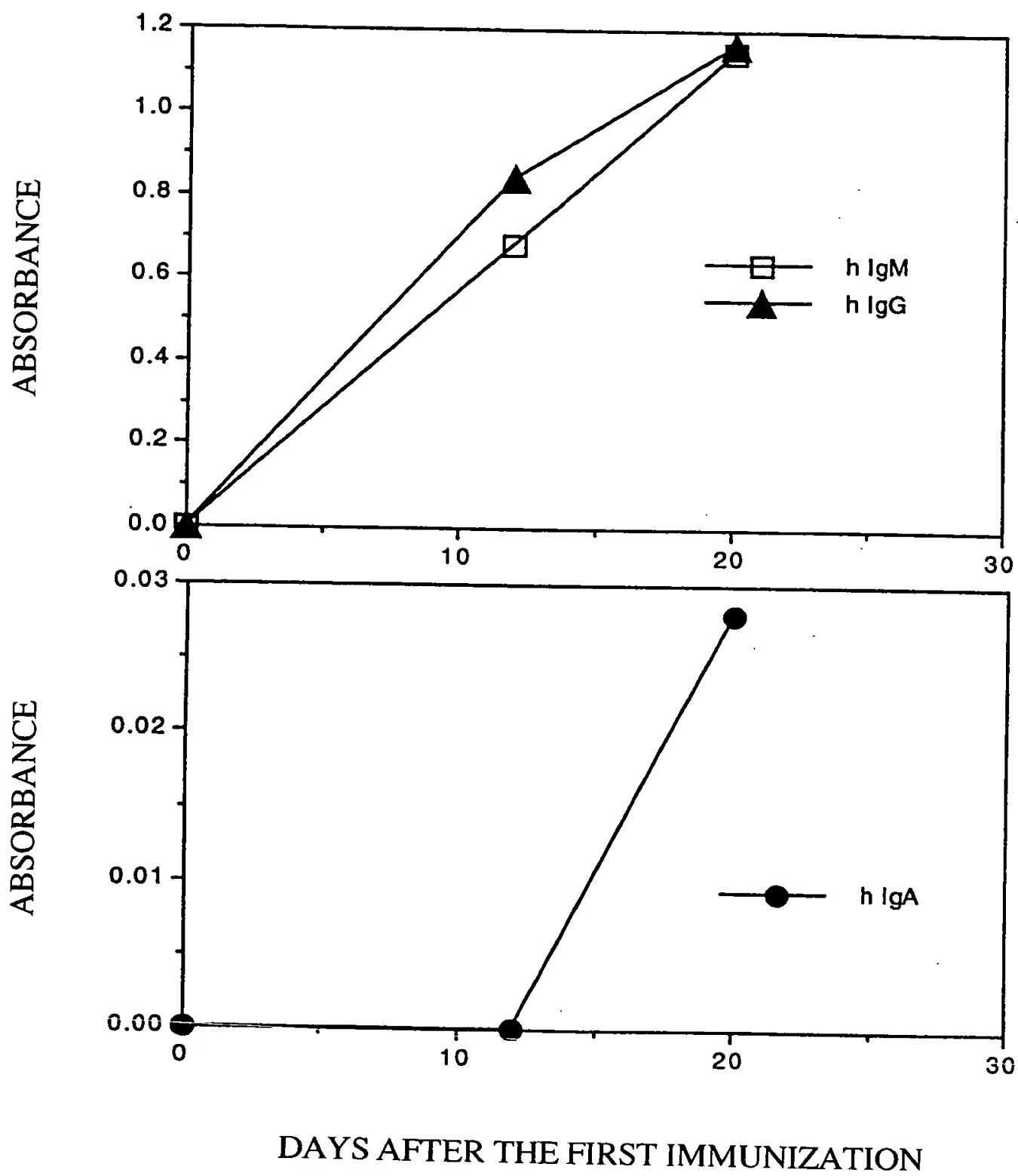


FIG. 33



CHROMOSOMES

Inventor(s): Kazuma TOMIZUKA et
al.

DOCKET NO.: 081356/0158

09/763362

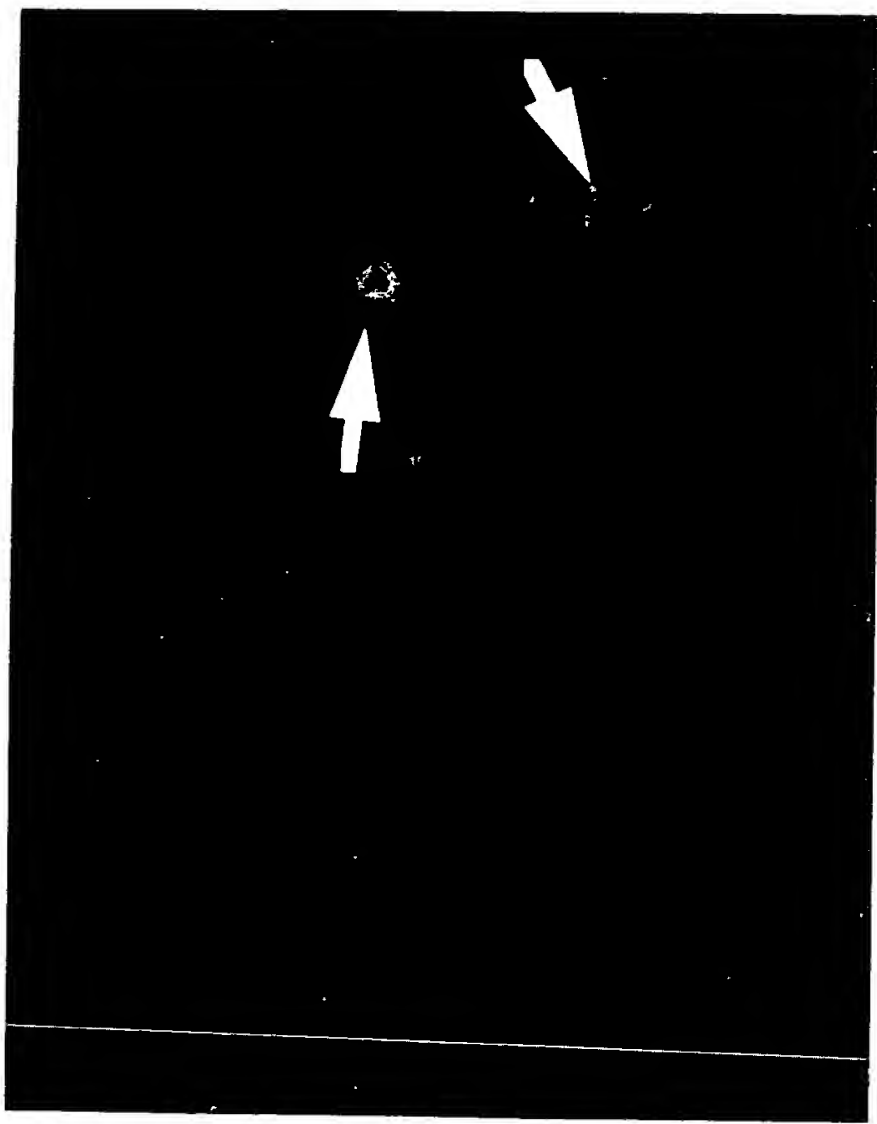
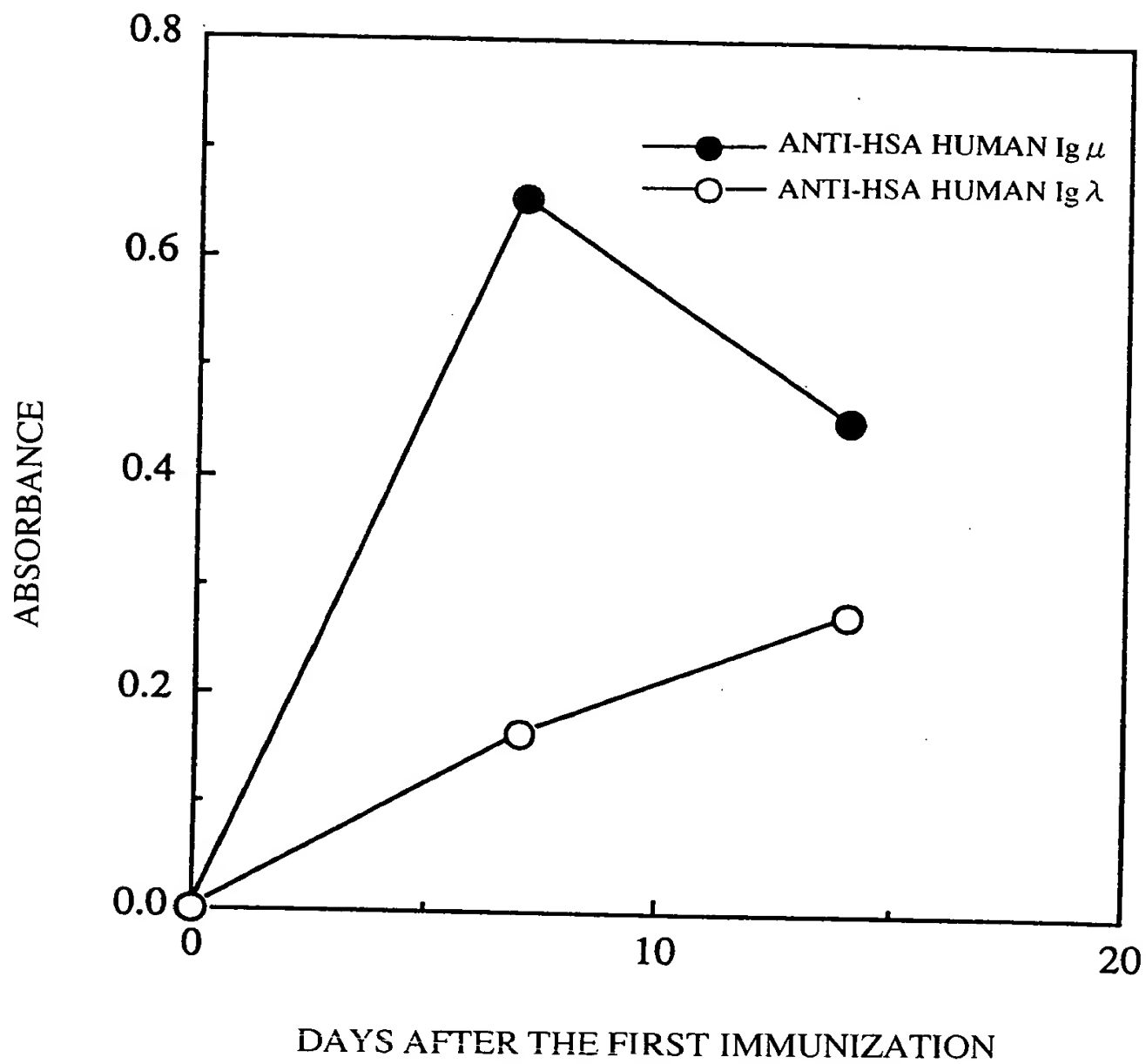


FIG. 34

FIG. 35



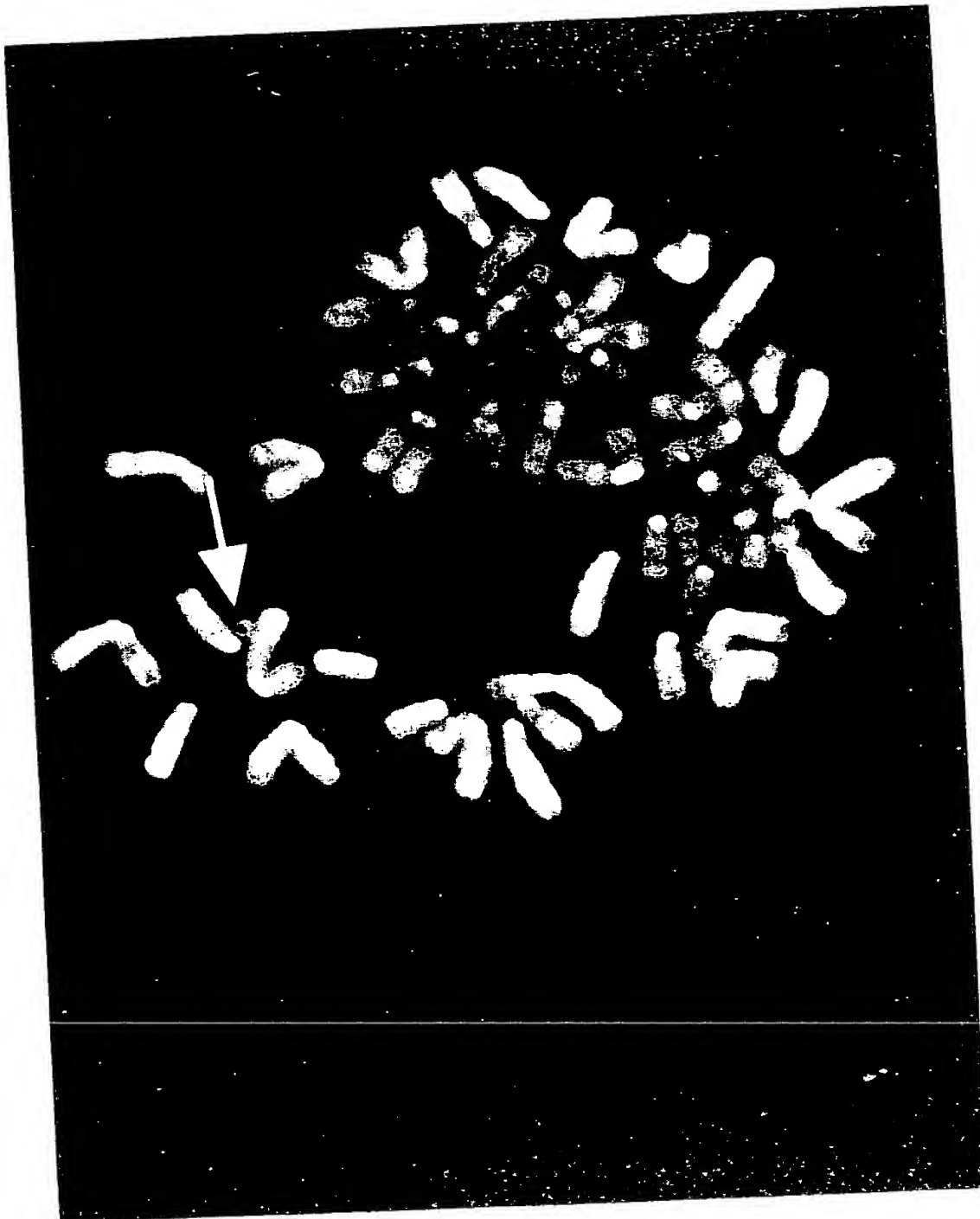


FIG. 36

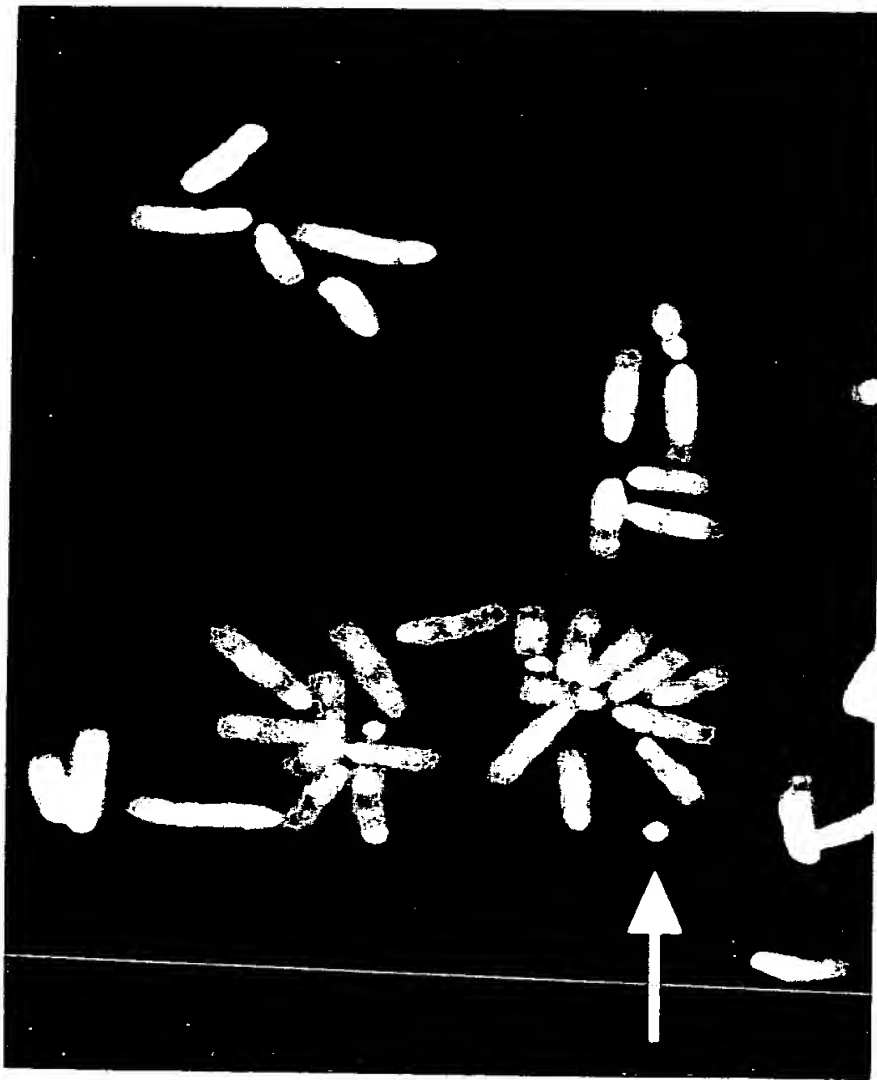


FIG. 37

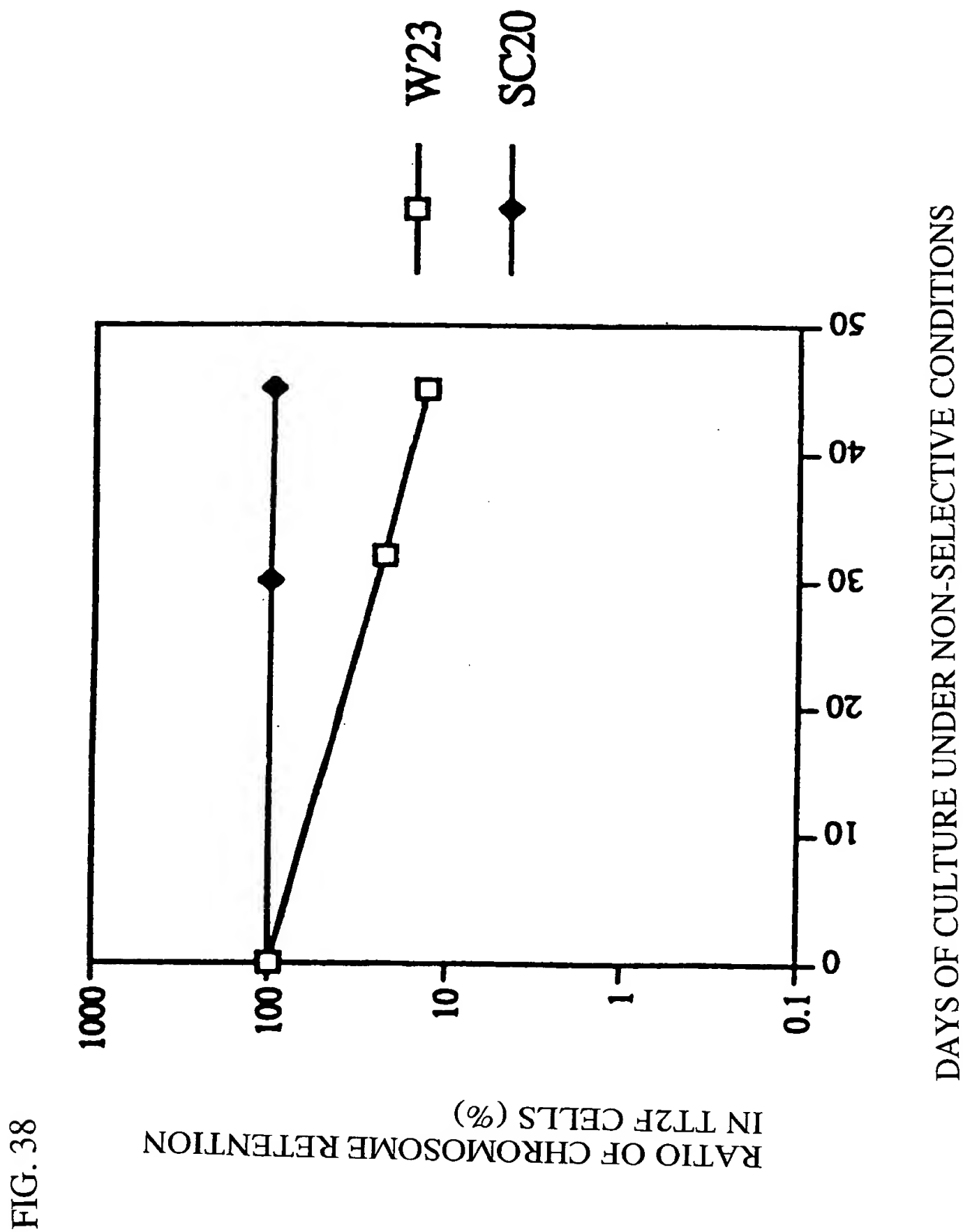


FIG. 39

	BRAIN		SPLEEN		LIVER		BONE MARROW		TESTIS					
									1ST MEIOSIS		2ND MEIOSIS		SPERM	
									+	-	+	-	+	-
16-5 (F1)	30 (100%)	-	11 (21%)	42	30 (97%)	1	1 (3%)	30	15 (100%)	0	15 (94%)	1	11 (32%)	23
17-8 (F1)	30 (100%)	0	12 (30%)	28	30 (100%)	0	21 (43%)	28	16 (100%)	0	9 (53%)	7	14 (34%)	27
17-23 (F1)	41 (95%)	2	7 (17%)	34	31 (97%)	1	5 (17%)	25	15 (100%)	0	13 (81%)	3	13 (52%)	12

RETENTION OF SC20 FRAGMENT IN MICE

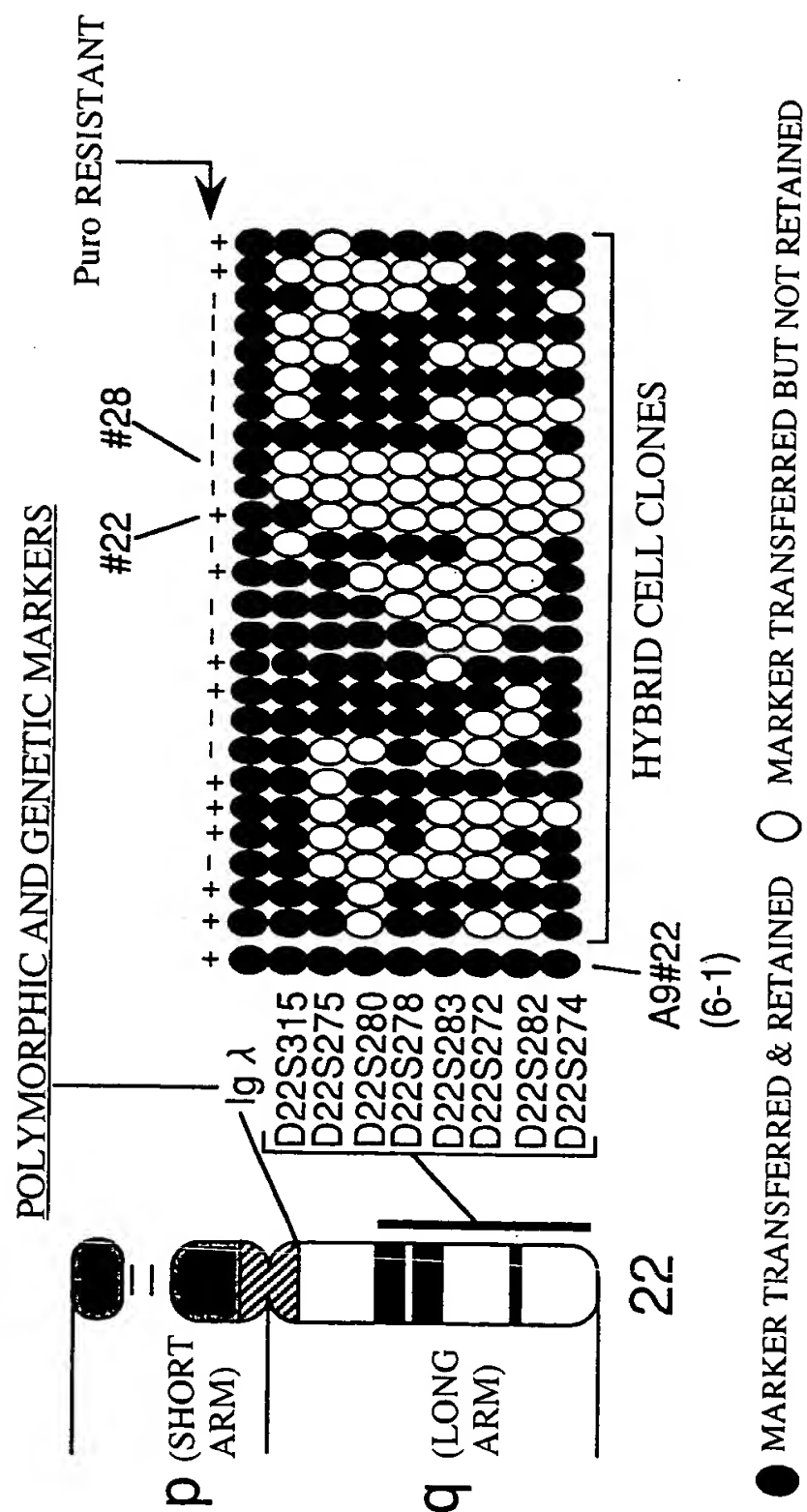
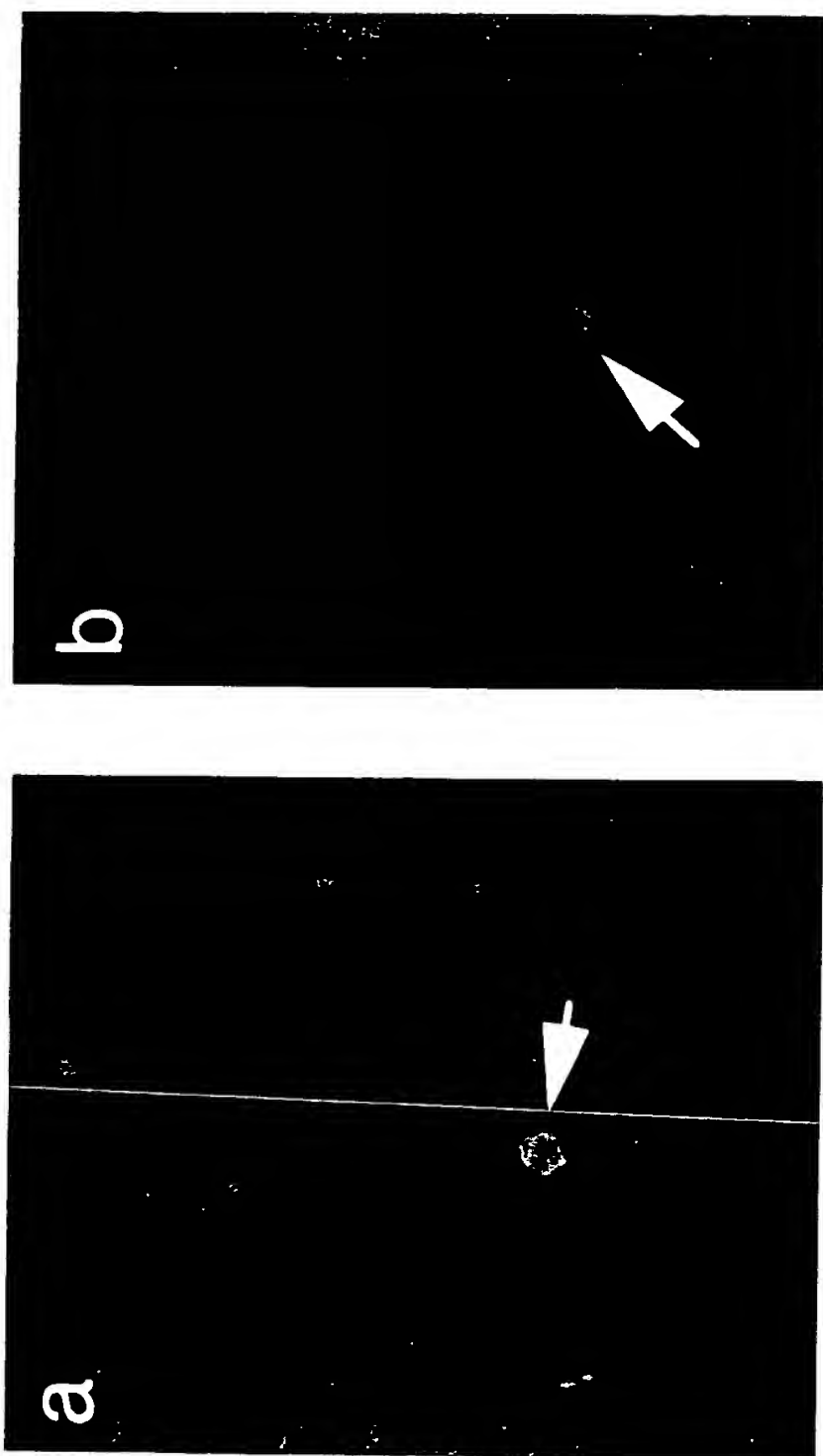


FIG. 40



b) CONTROL

a) CLONE #28

FIG. 41

	HK23	HK28	HK29
ANTIBODY HEAVY-CHAIN KNOCKOUT	HOMO	WILD-TYPE OR HETERO	WILD-TYPE OR HETERO
ANTIBODY LIGHT-CHAIN KNOCKOUT	HETERO	WILD-TYPE	HETERO
W23 FRAGMENT	+	+	+
SC20 FRAGMENT	+	+	+
HUMAN μ CHAIN IN SERUM (mg/l)	100	5.9	14
HUMAN κ CHAIN IN SERUM (mg/l)	8.6	8.4	25
HUMAN μ/κ CHAINS IN SERUM (mg/l)	18	0.13	BELOW DETECTION LIMIT

* SINCE "ANTIBODY HEAVY-CHAIN KNOCKOUT" IS JUDGED BY THE PRESENCE OR ABSENCE OF THE EXPRESSION OF MOUSE μ CHAIN, IT IS IMPOSSIBLE TO DISCRIMINATE HETERO FROM WILD-TYPE.

* "ANTIBODY LIGHT-CHAIN KNOCKOUT" IS JUDGED BY SOUTHERN BLOT ANALYSIS.

FIG. 42

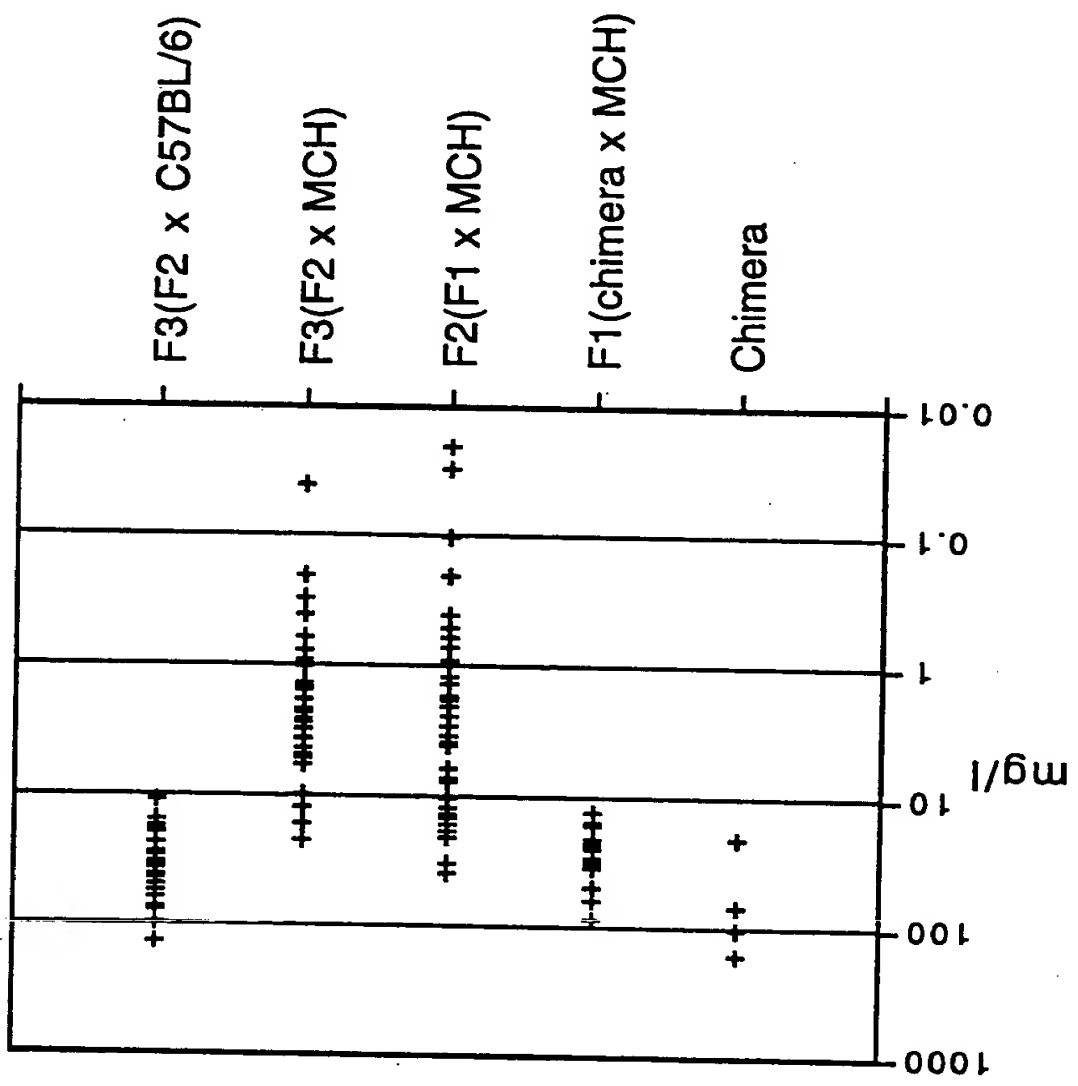
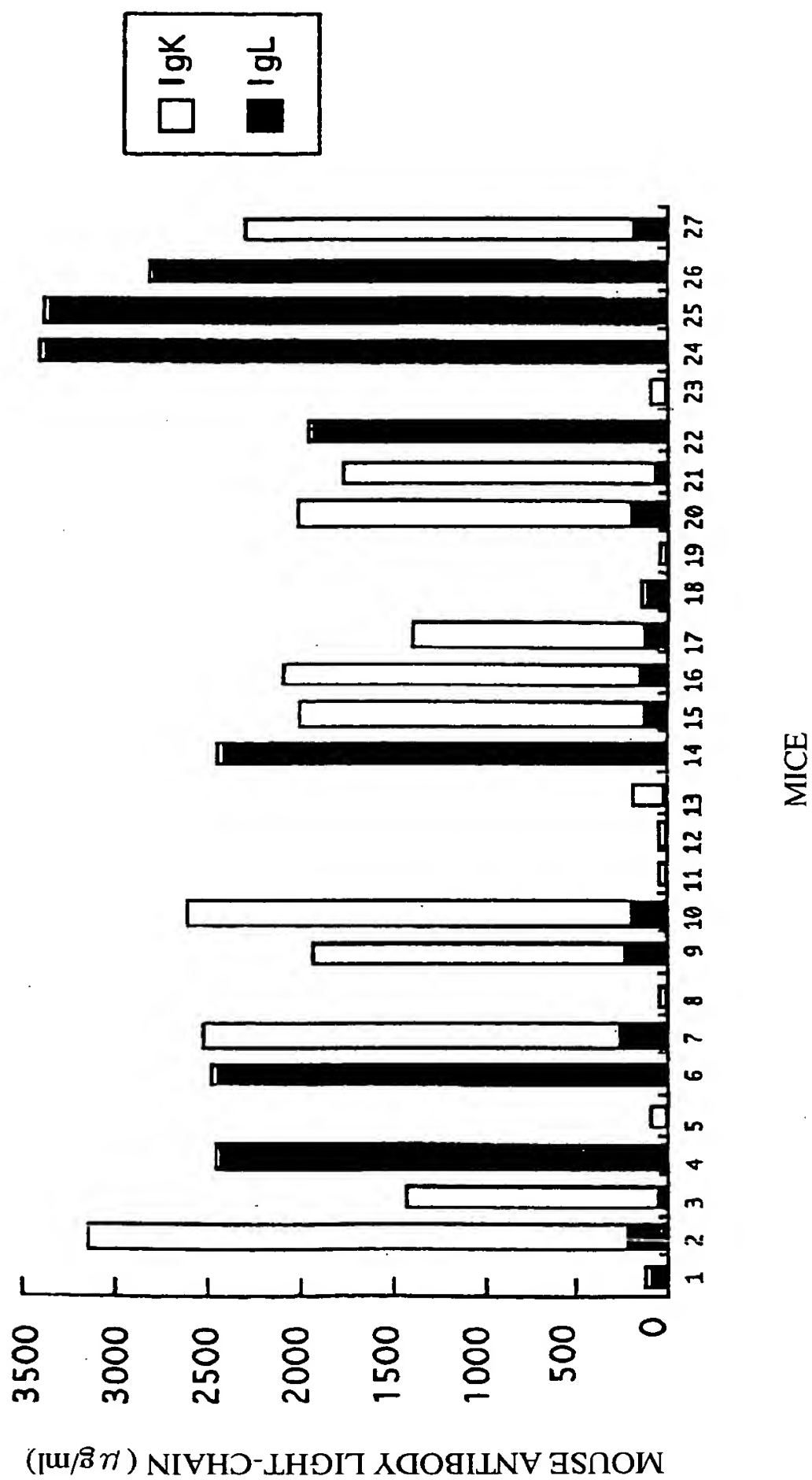


FIG. 43

FIG. 44



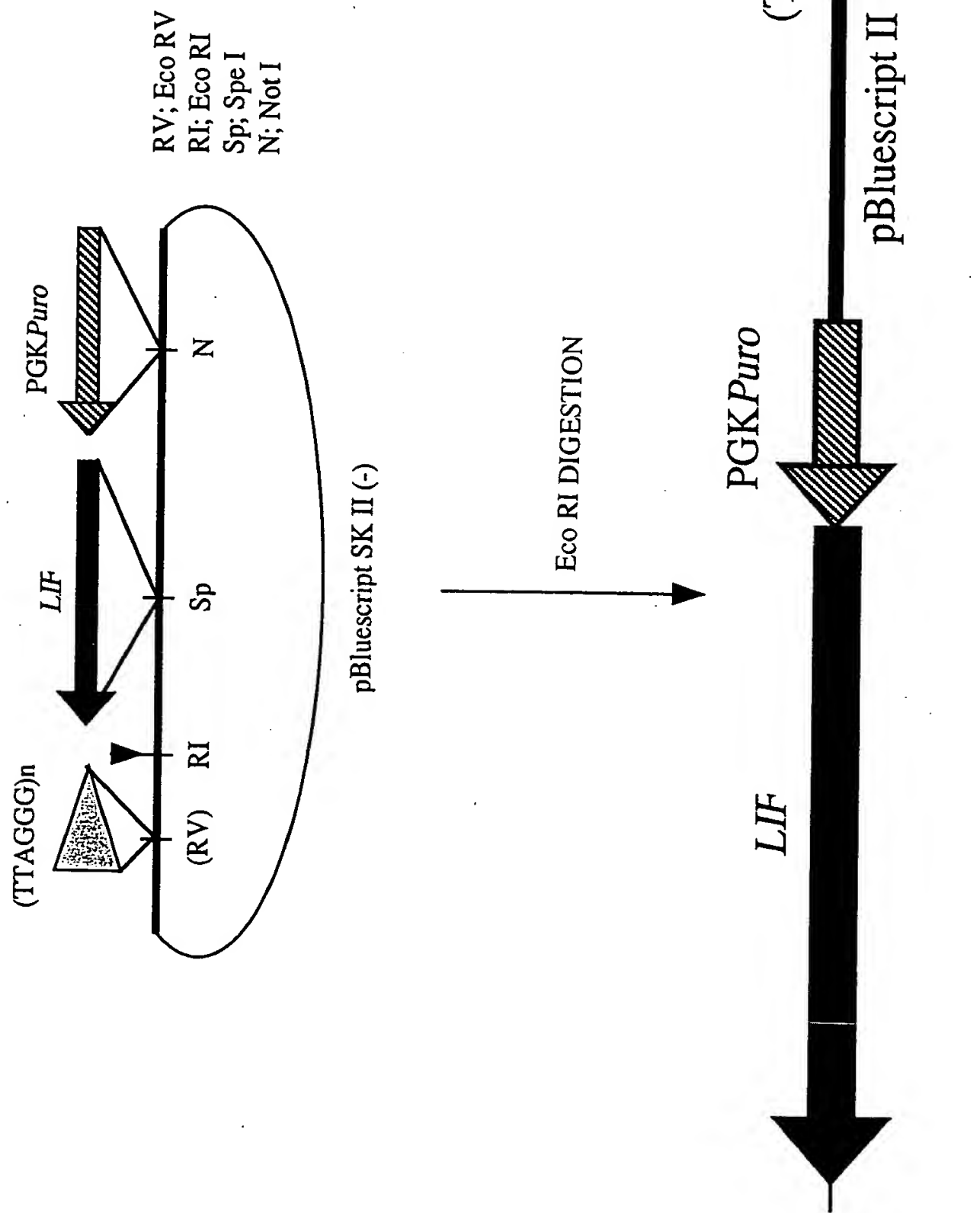


FIG. 45

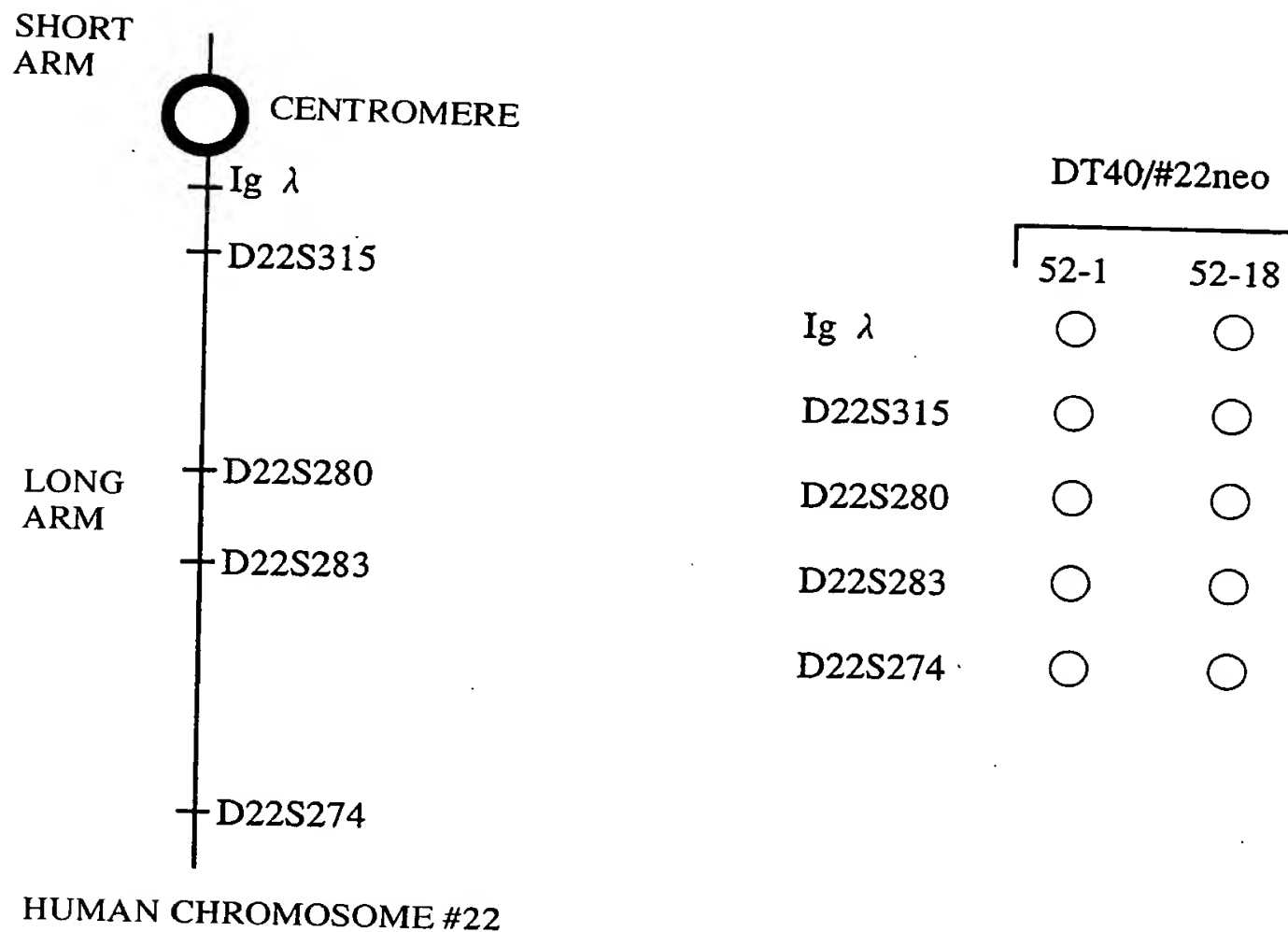


FIG. 46

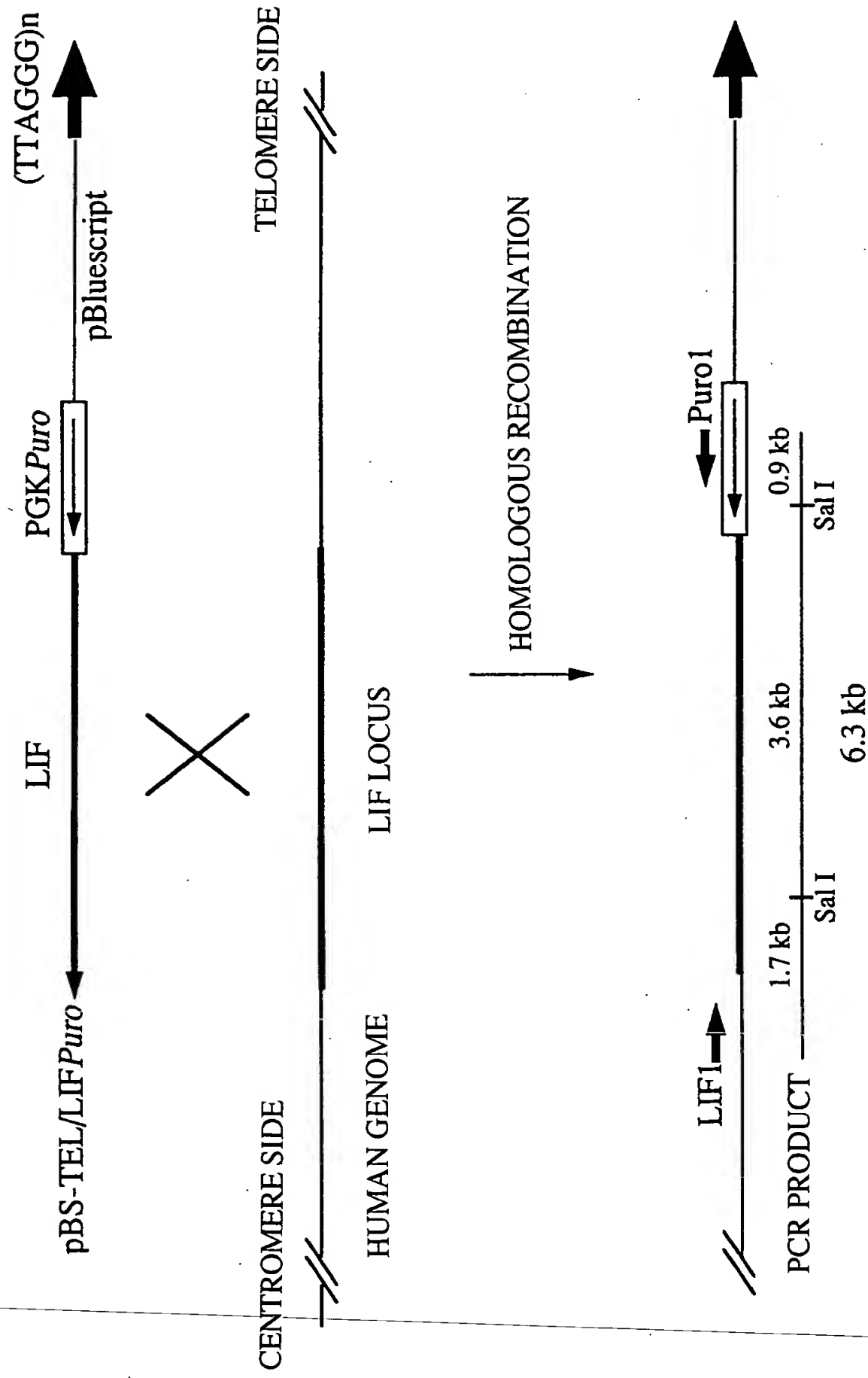


FIG. 47

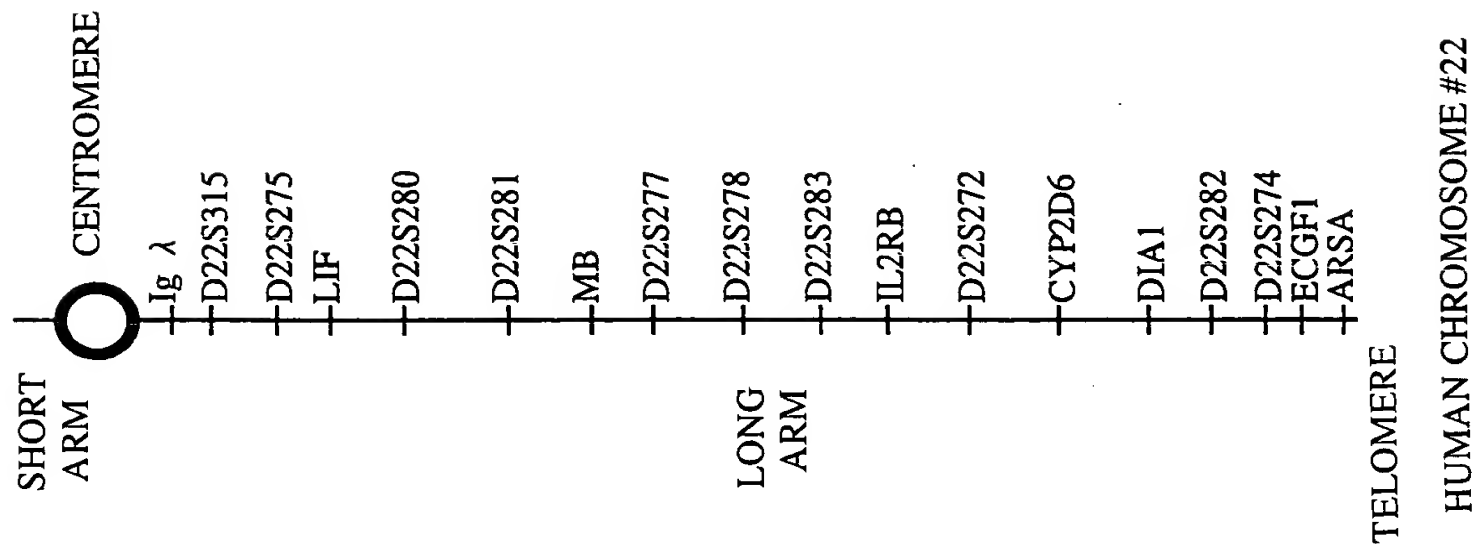


FIG. 48

	52-18	64	67	68	212	222	305	328	343
Ig λ	O	O	O	O	NT	NT	O	O	O
D22S315	O	O	O	O	NT	NT	O	O	O
D22S275	O	O	O	O	O	O	O	O	O
LIF	O	O	O	O	O	O	O	O	O
D22S280	O	O	X	X	NT	NT	O	X	X
D22S281	O	O	X	X	O	O	O	X	X
MB	O	X	X	X	X	O	O	X	X
D22S277	O	O	X	X	O	O	O	X	X
D22S278	O	O	X	X	O	O	O	X	X
D22S283	O	O	X	X	NT	NT	O	X	X
IL2RB	O	O	X	X	O	O	O	X	X
D22S272	O	O	X	X	O	O	O	X	X
CYP2D6	O	O	X	X	O	O	O	X	X
DIA1	O	O	X	X	O	O	O	X	X
D22S282	O	X	X	X	X	X	O	X	X
D22S274	O	O	X	X	NT	NT	O	X	X
ECGF1	O	O	X	X	O	O	O	X	X
ARSA	O	O	X	X	O	O	O	X	X

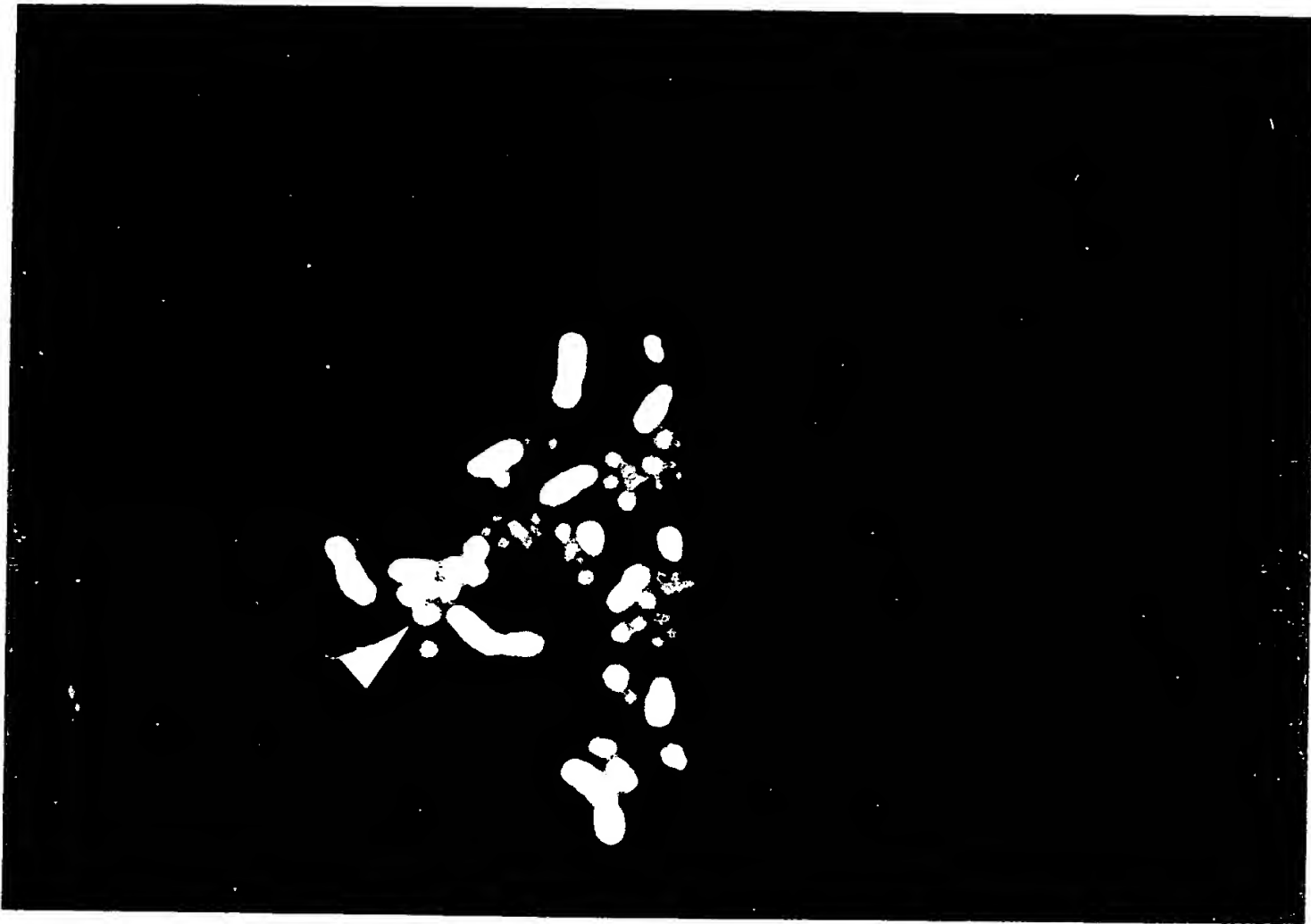


FIG. 49

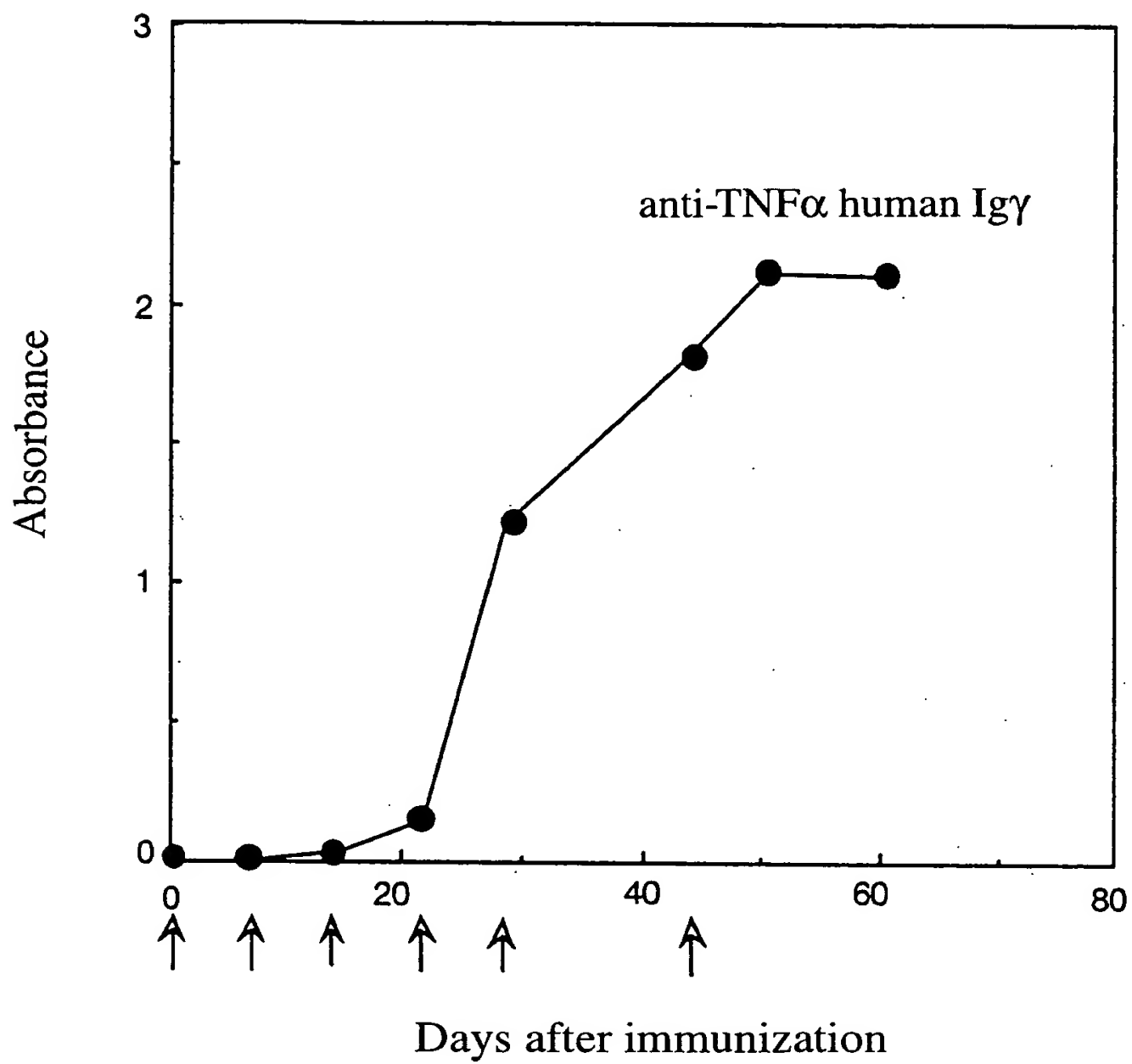


FIG. 50

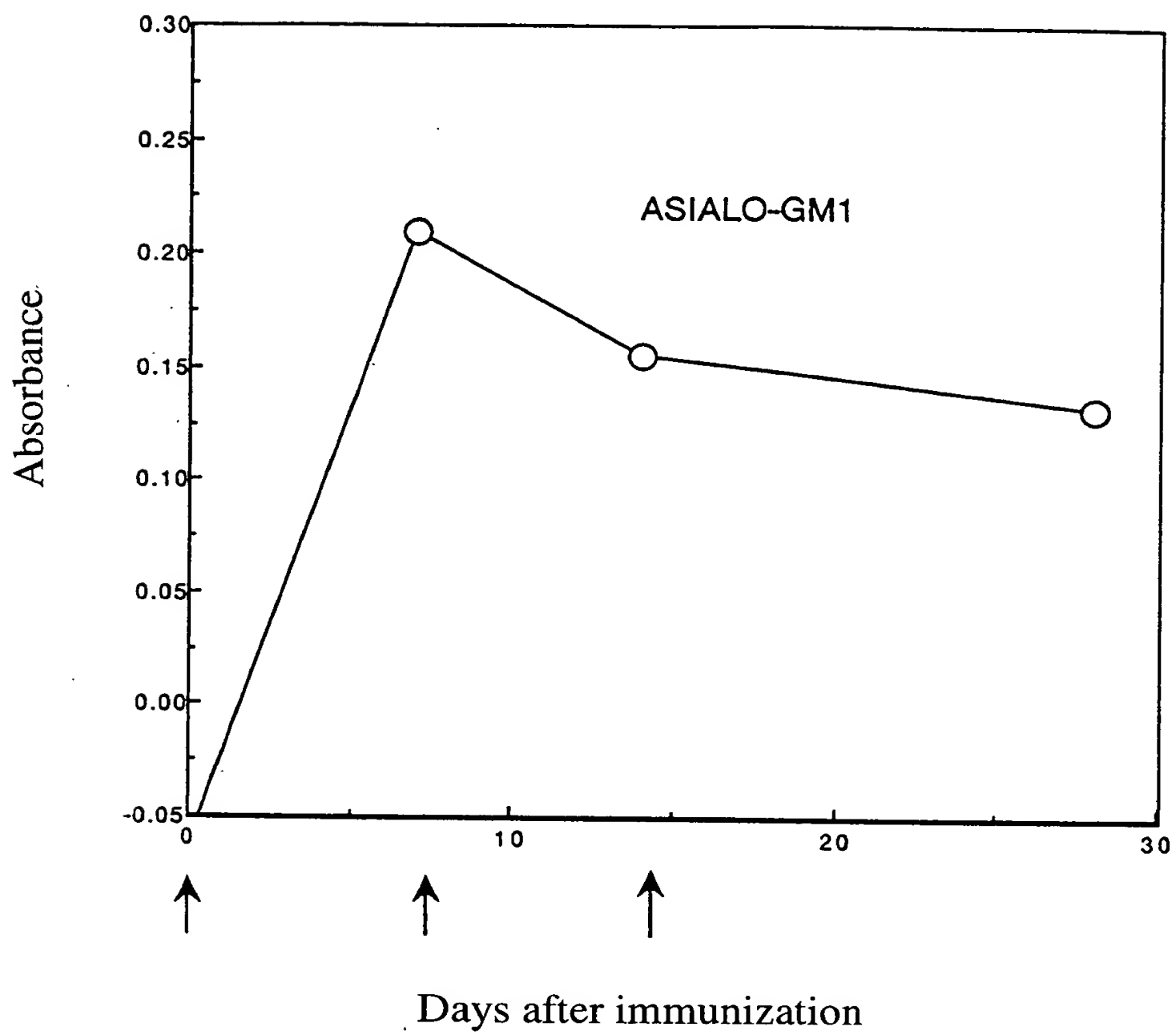


FIG. 51

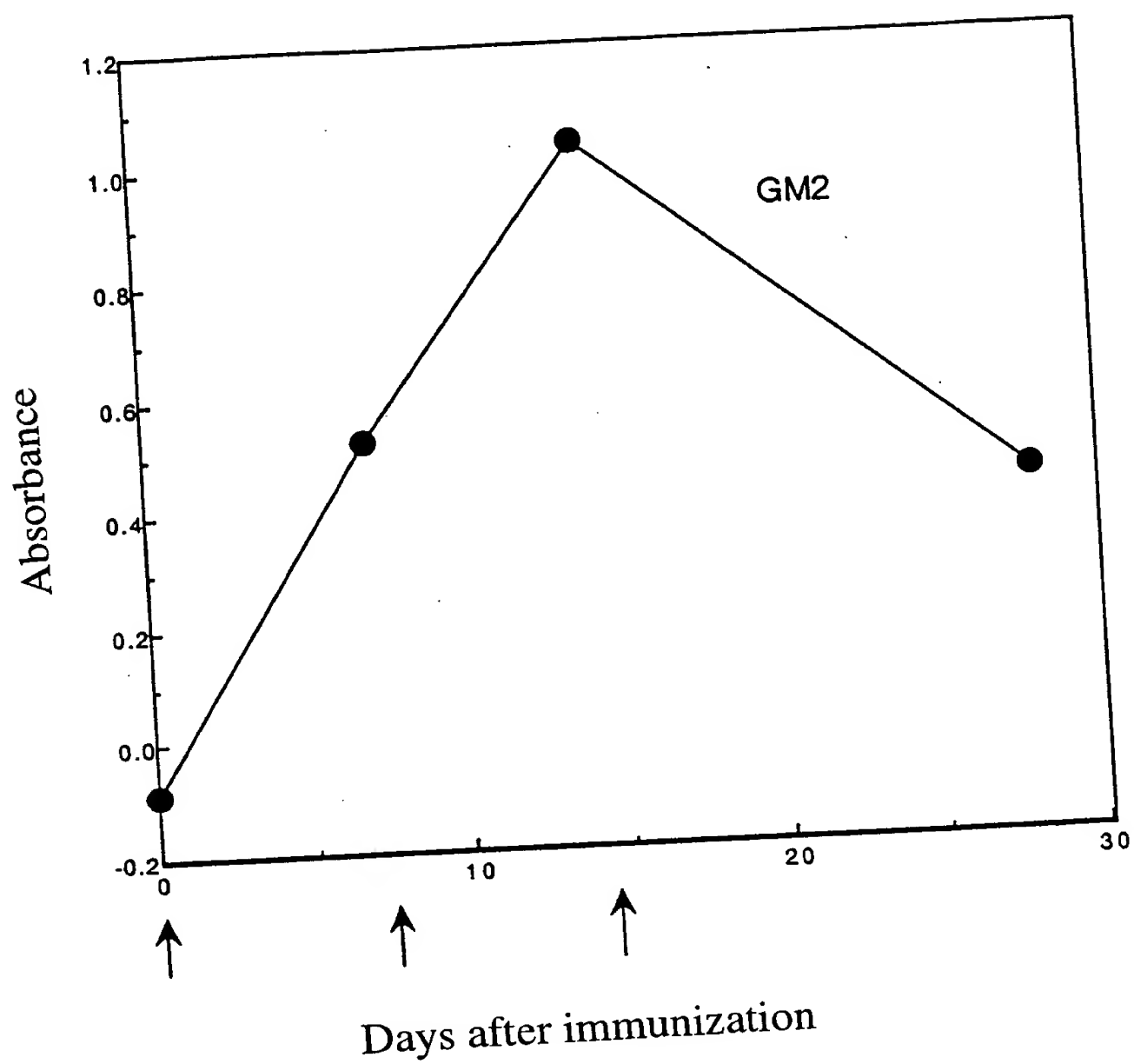
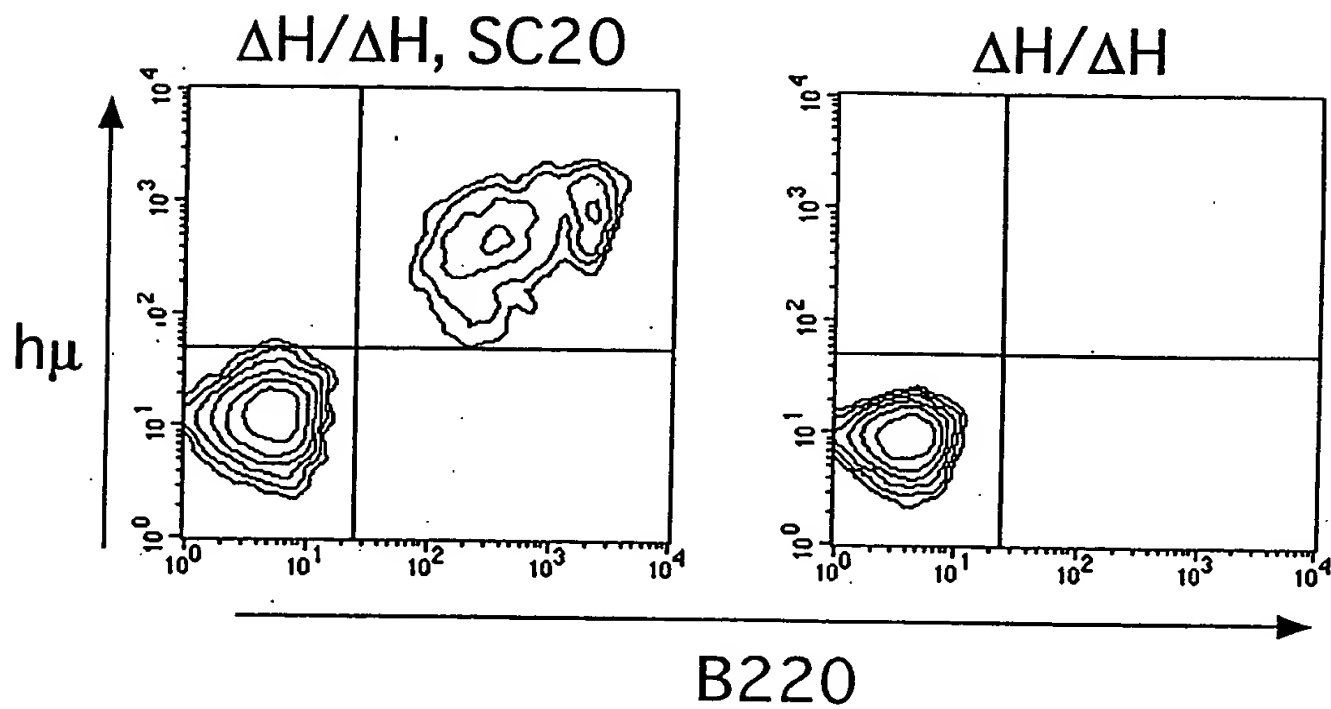


FIG. 52



$\Delta H/\Delta H, SC20$: Single Tc/KO mouse

$\Delta H/\Delta H$: antibody heavy-chain KO mouse

FIG. 53

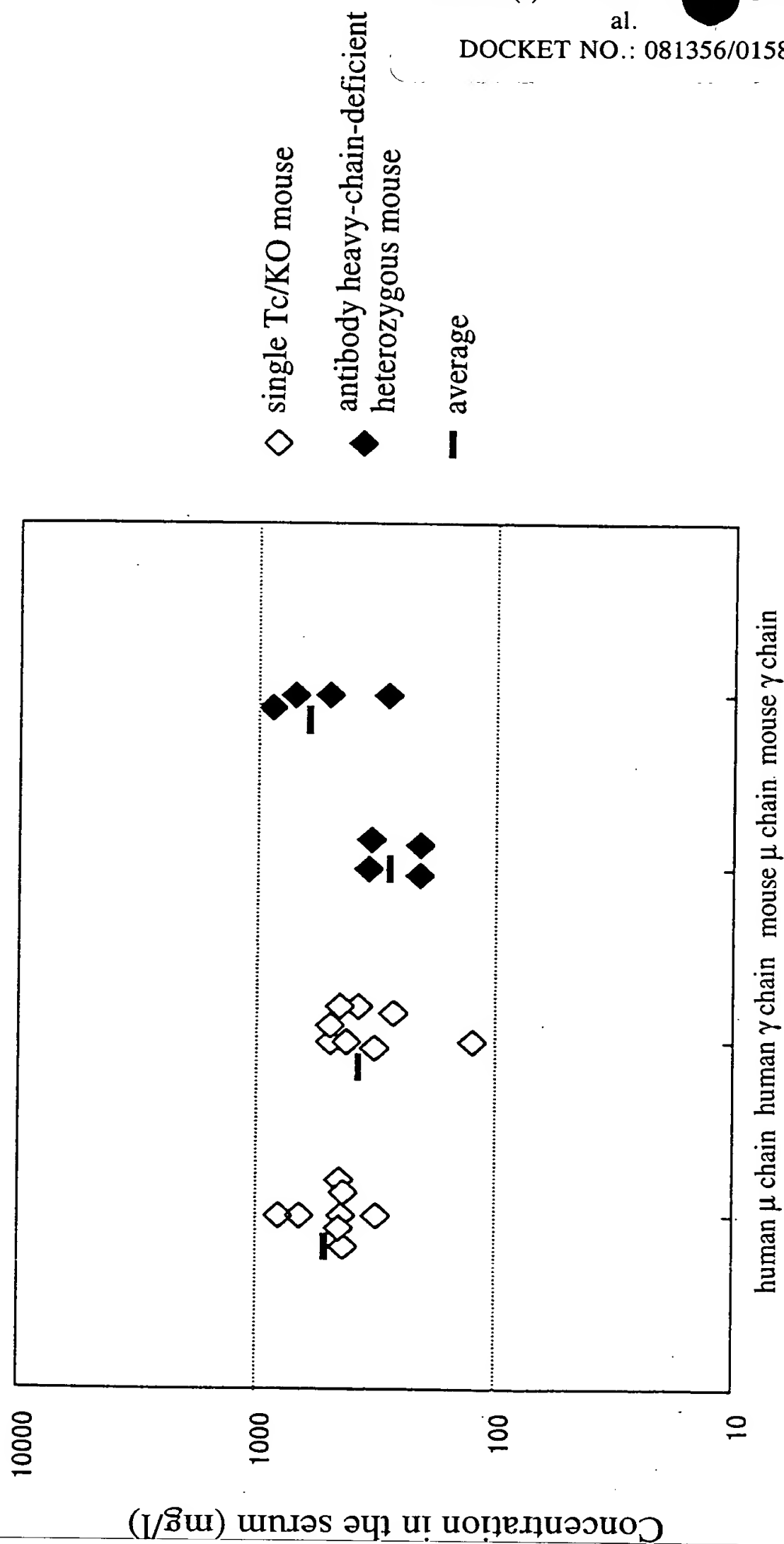


FIG. 54

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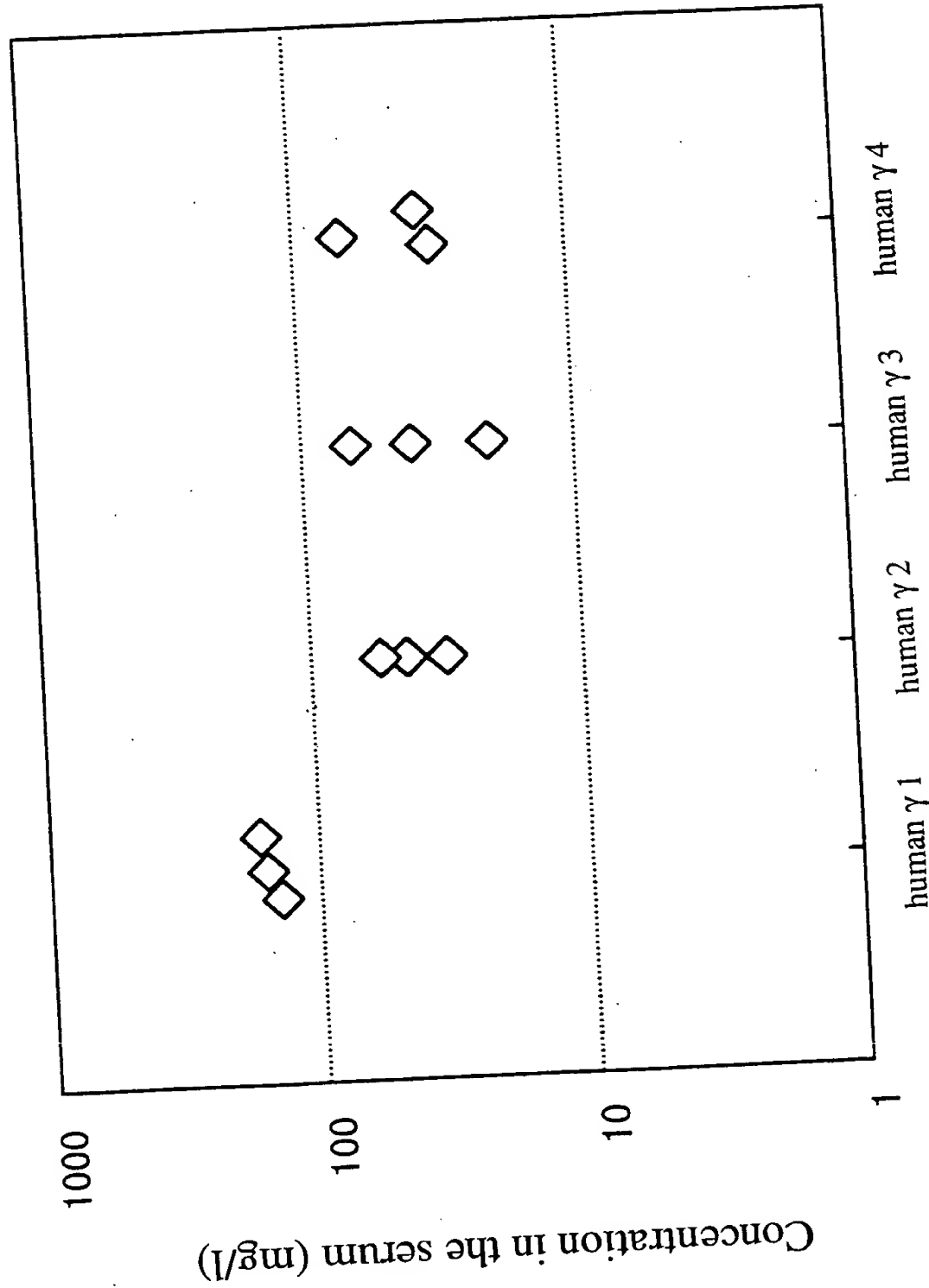


FIG. 55

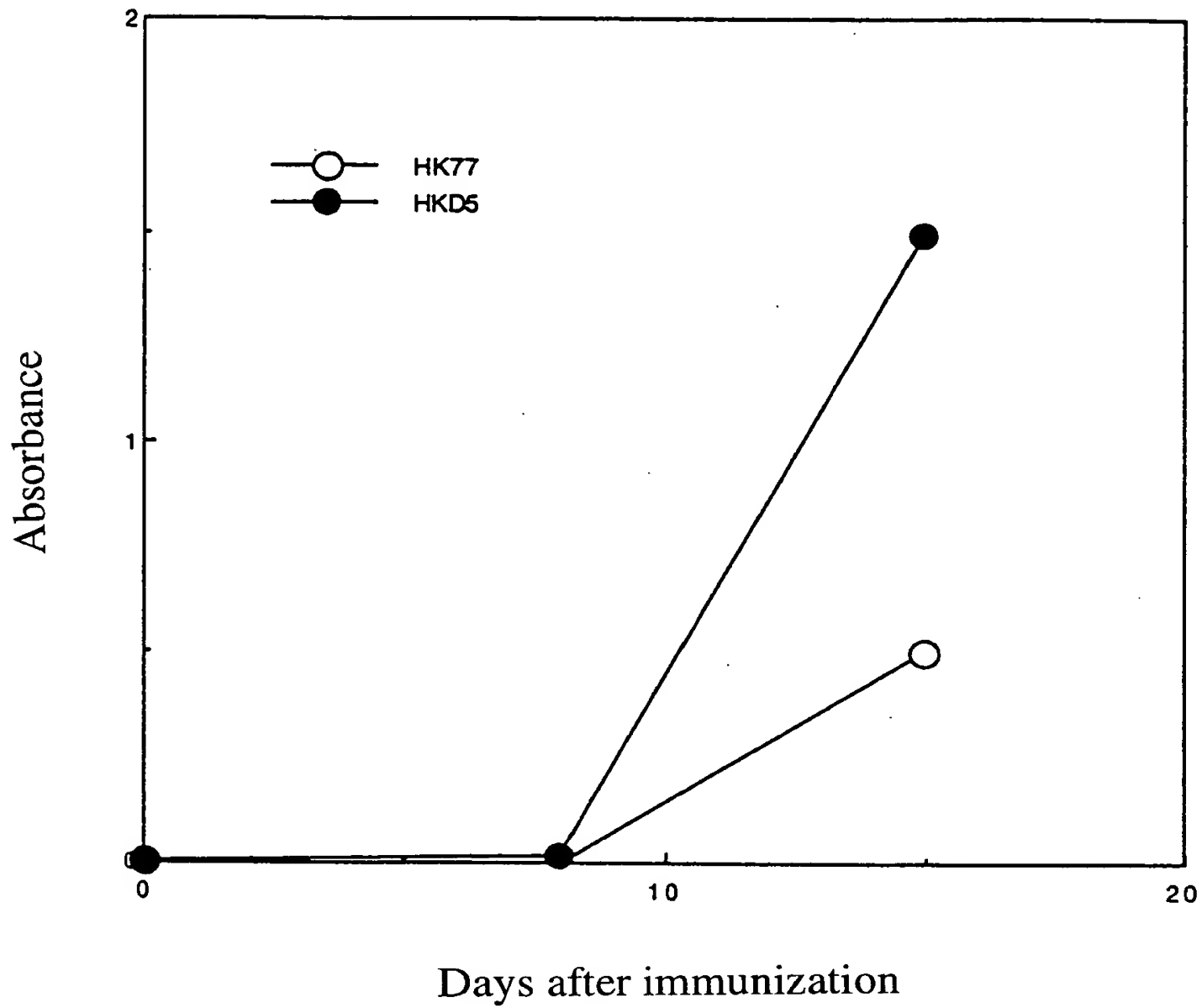


FIG. 56

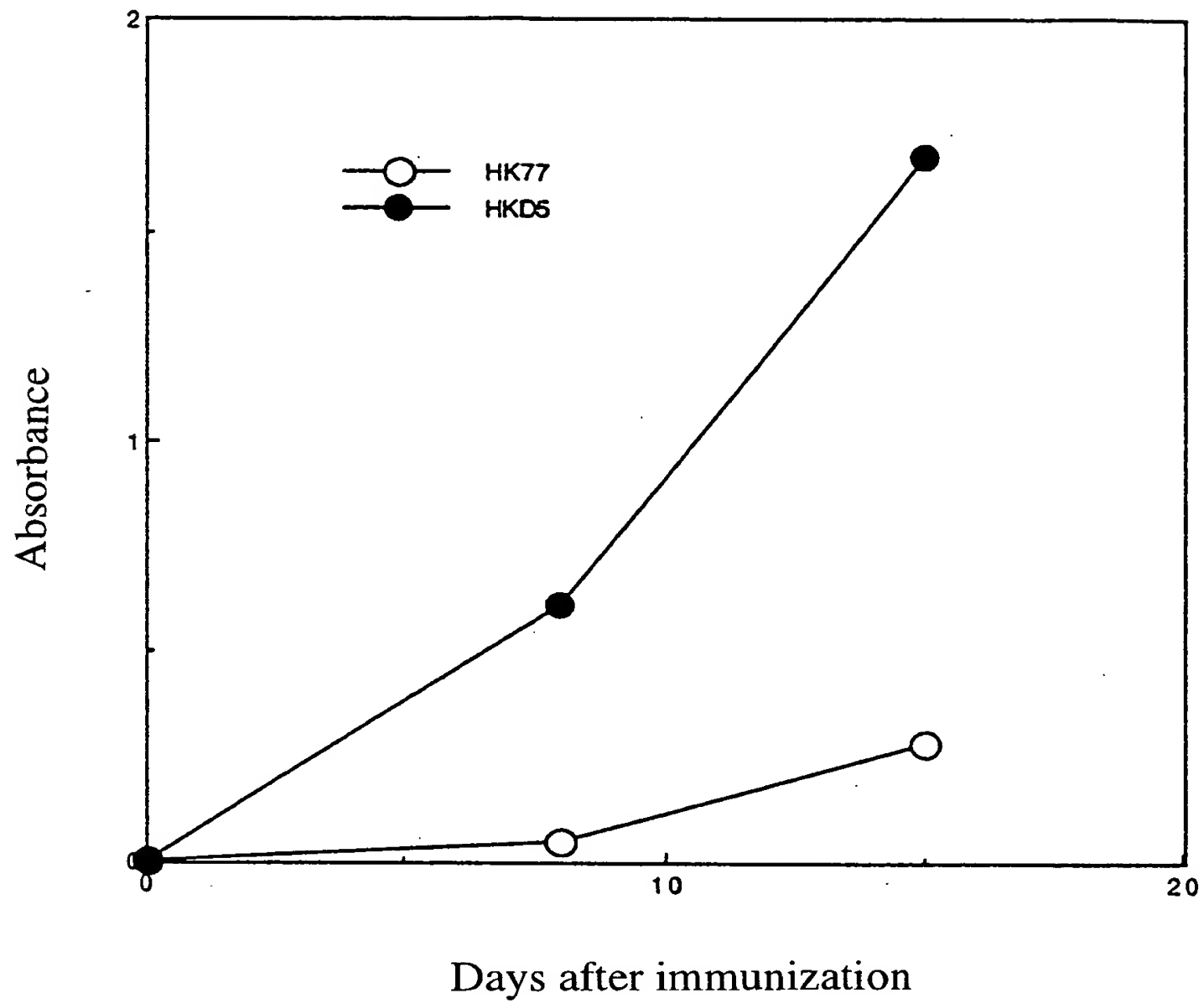


FIG. 57

FIG. 58

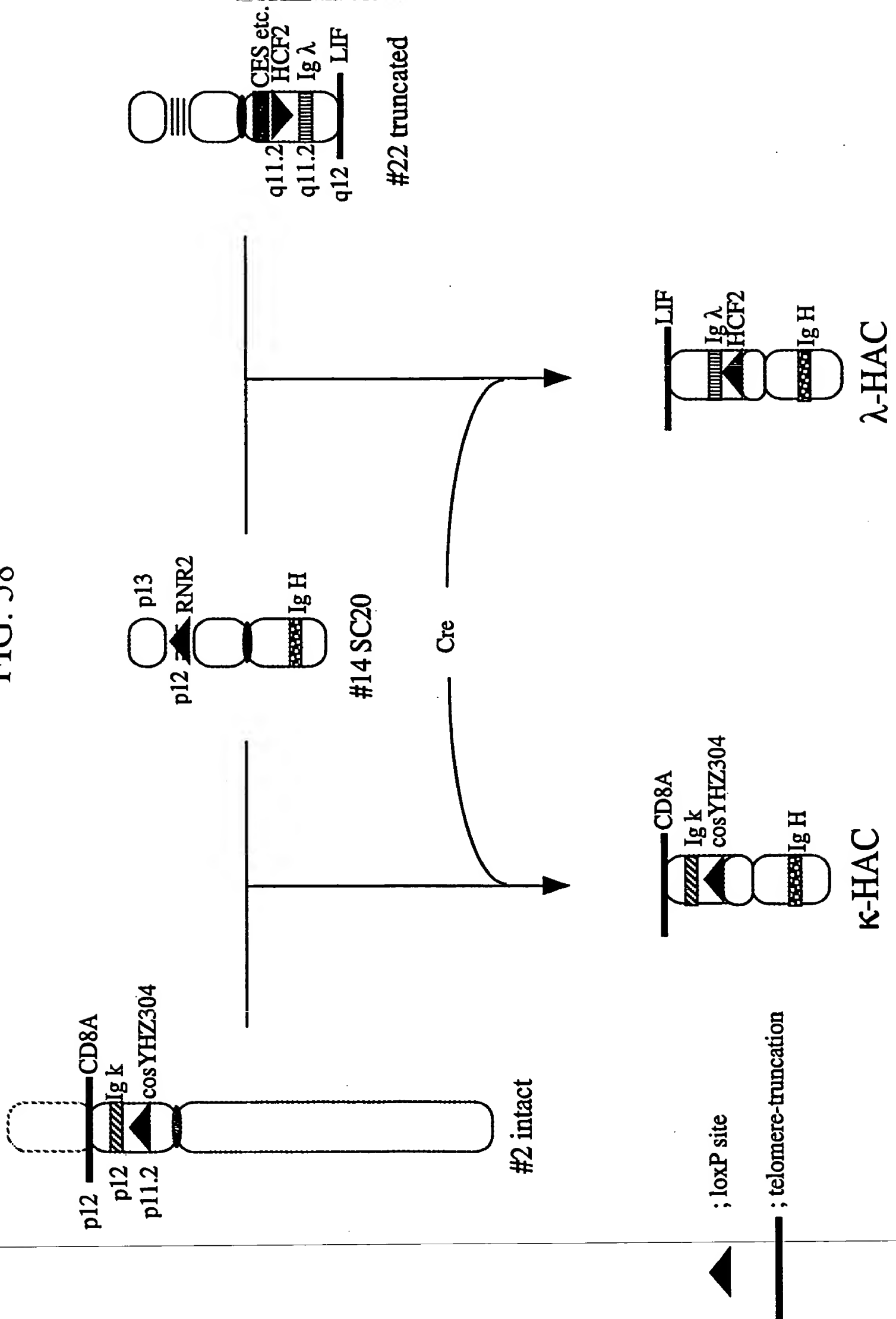


FIG. 59

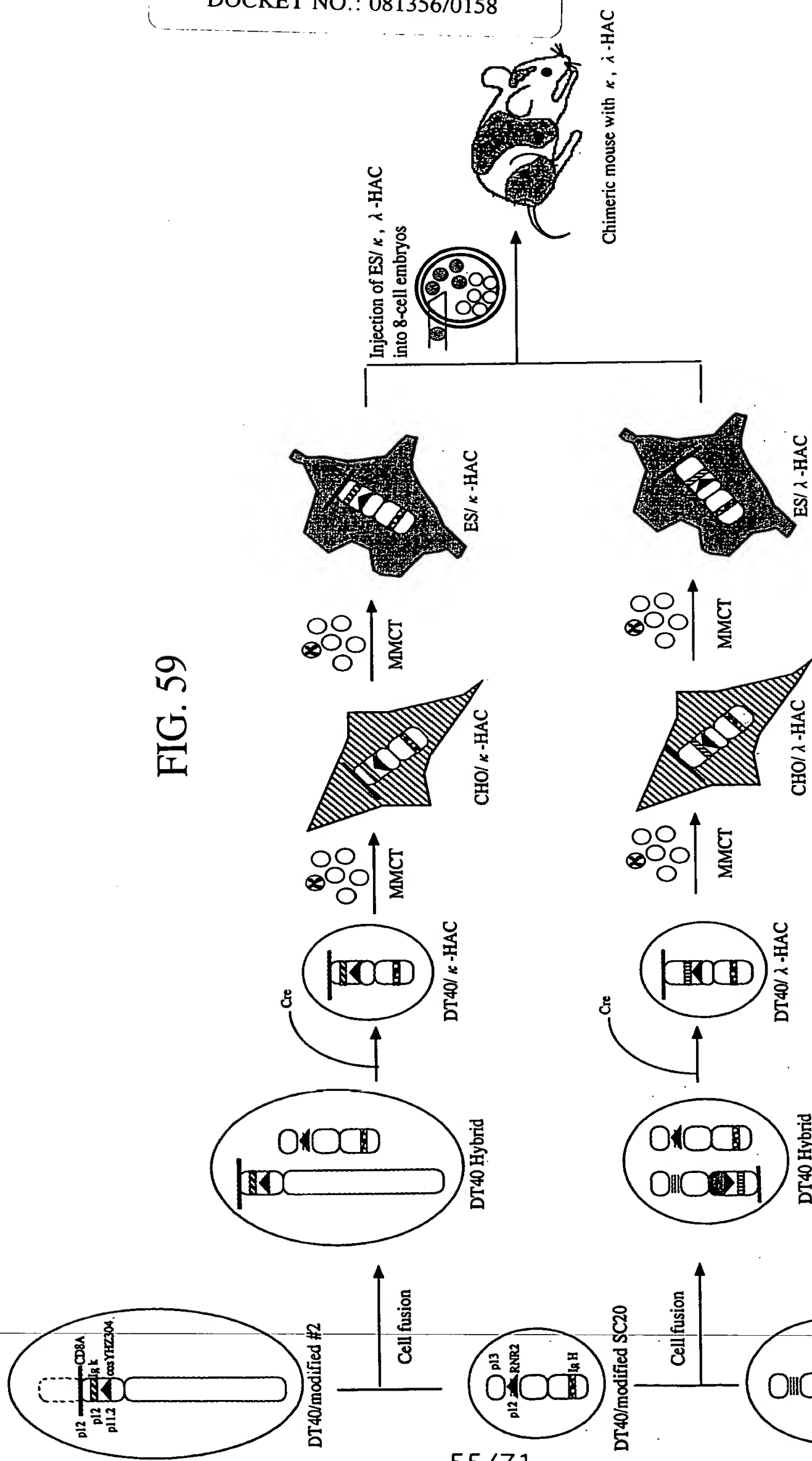
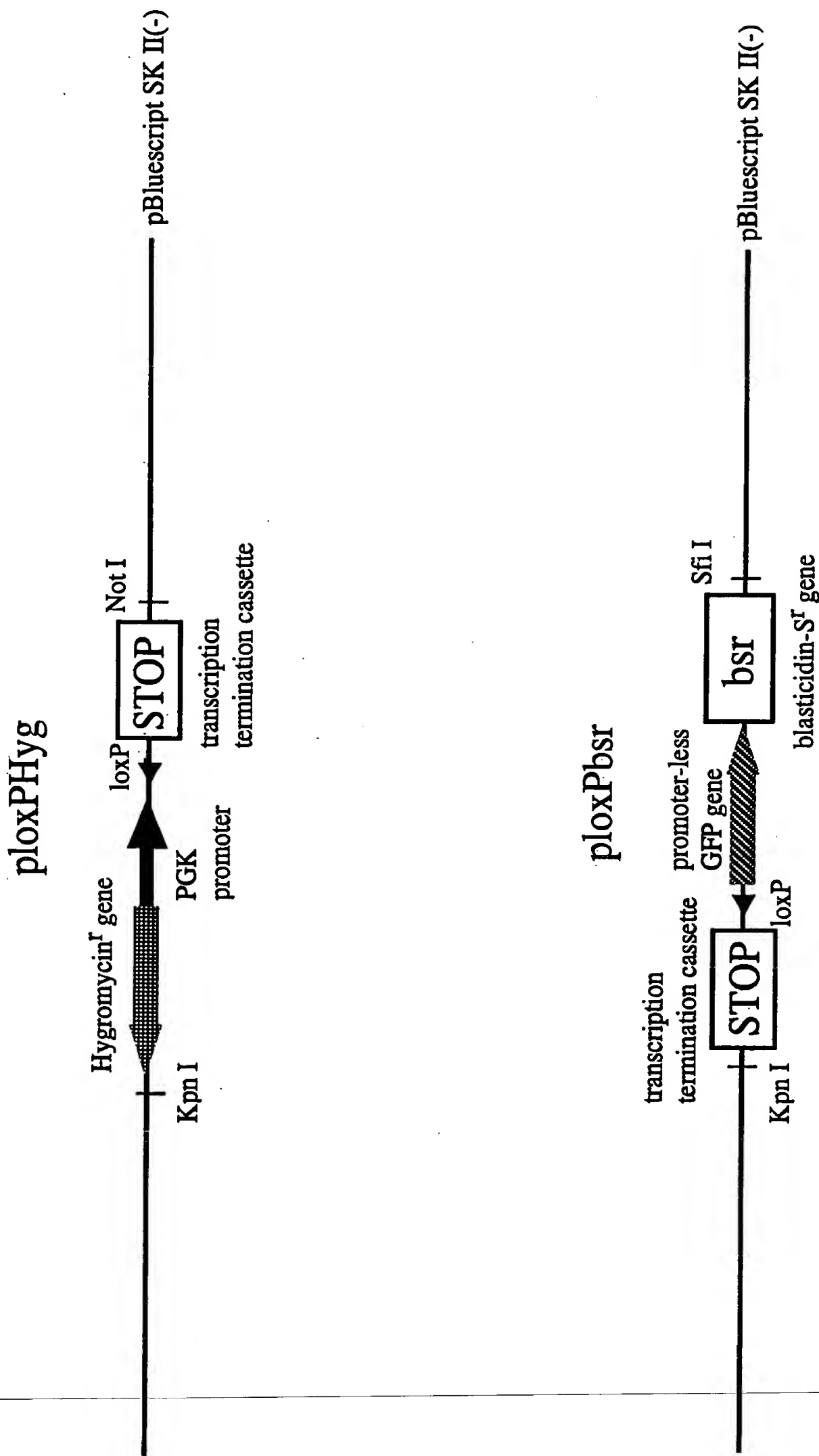


FIG. 60



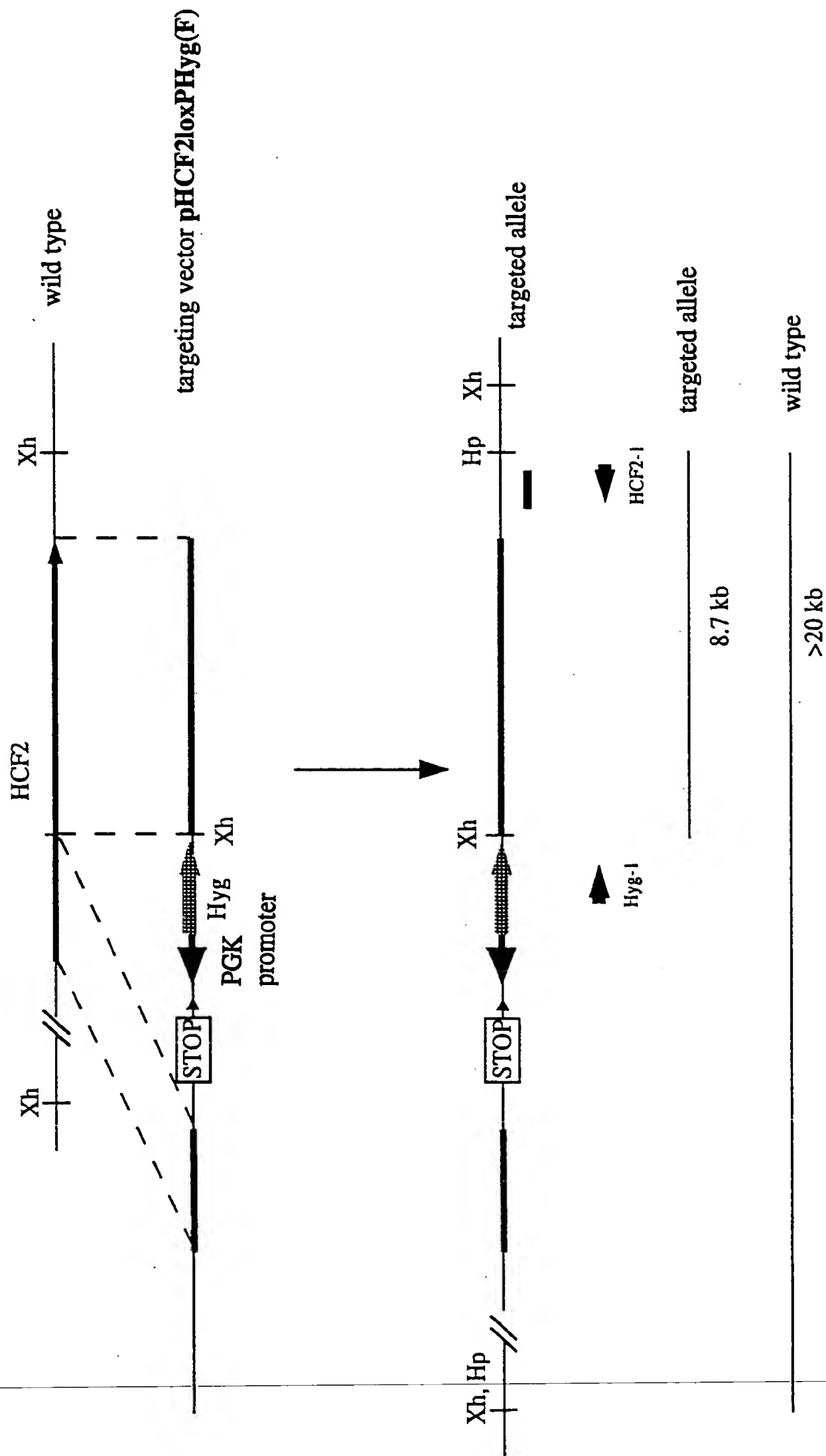


FIG. 61

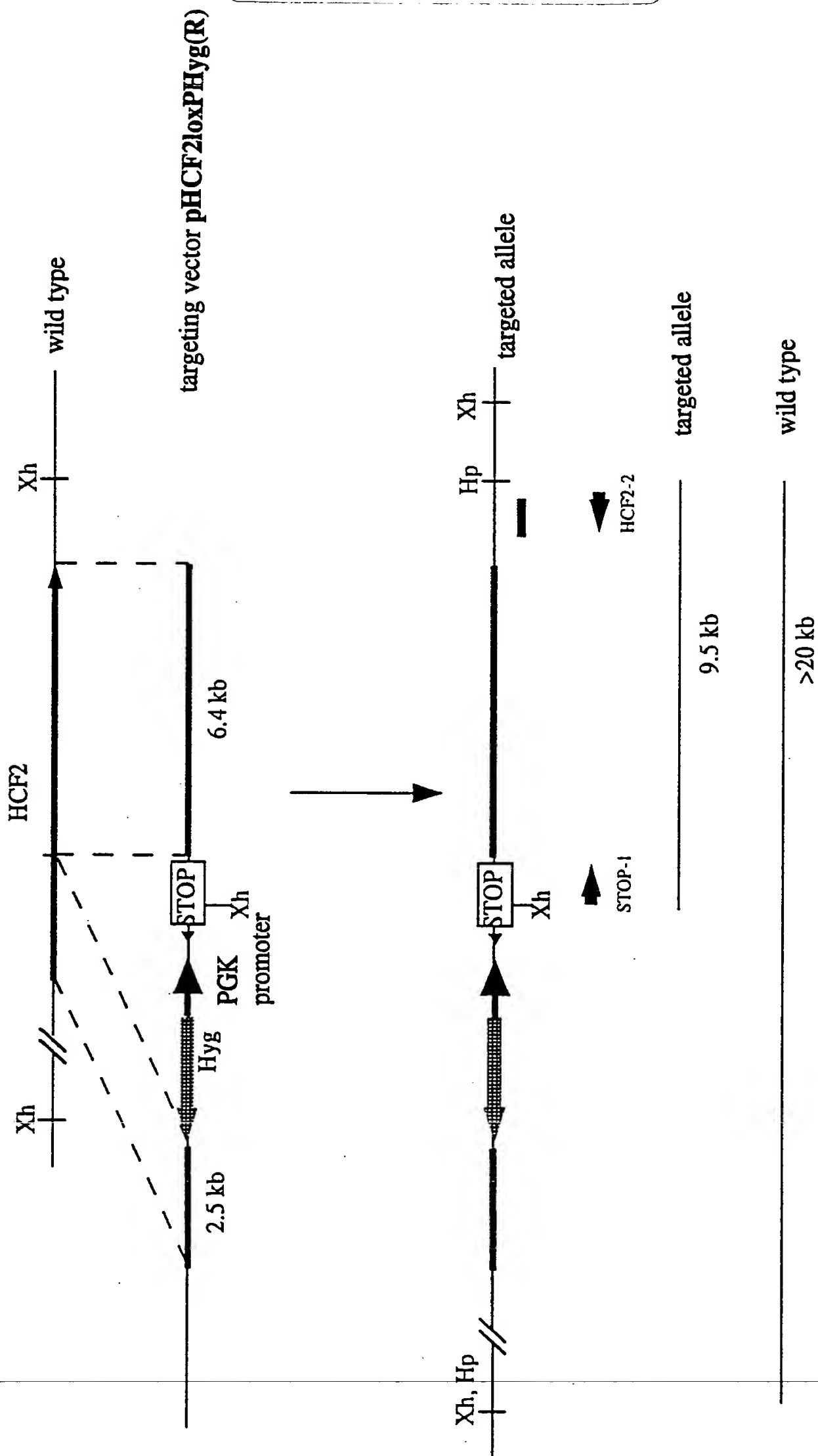


FIG. 62

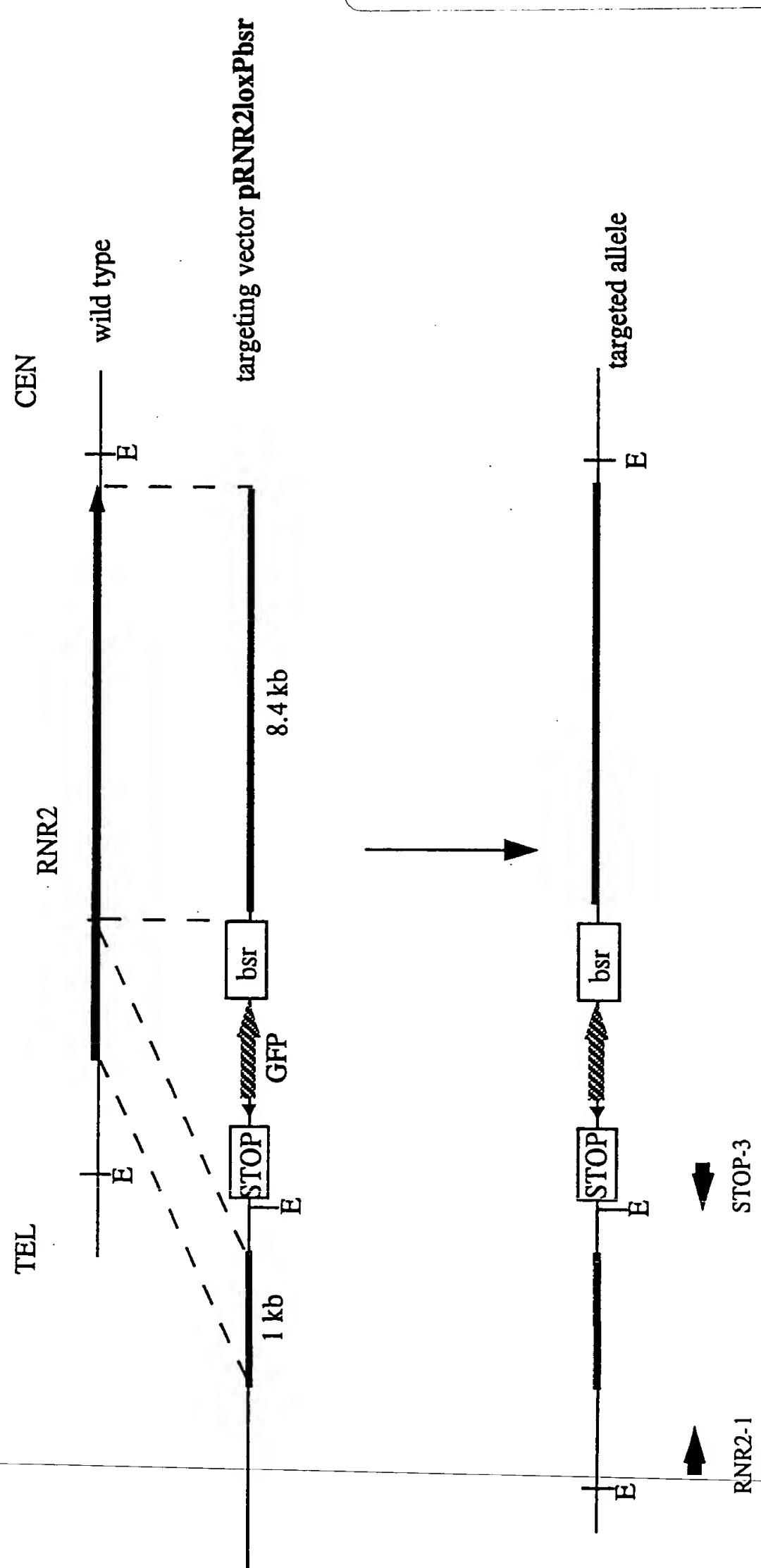


FIG. 63

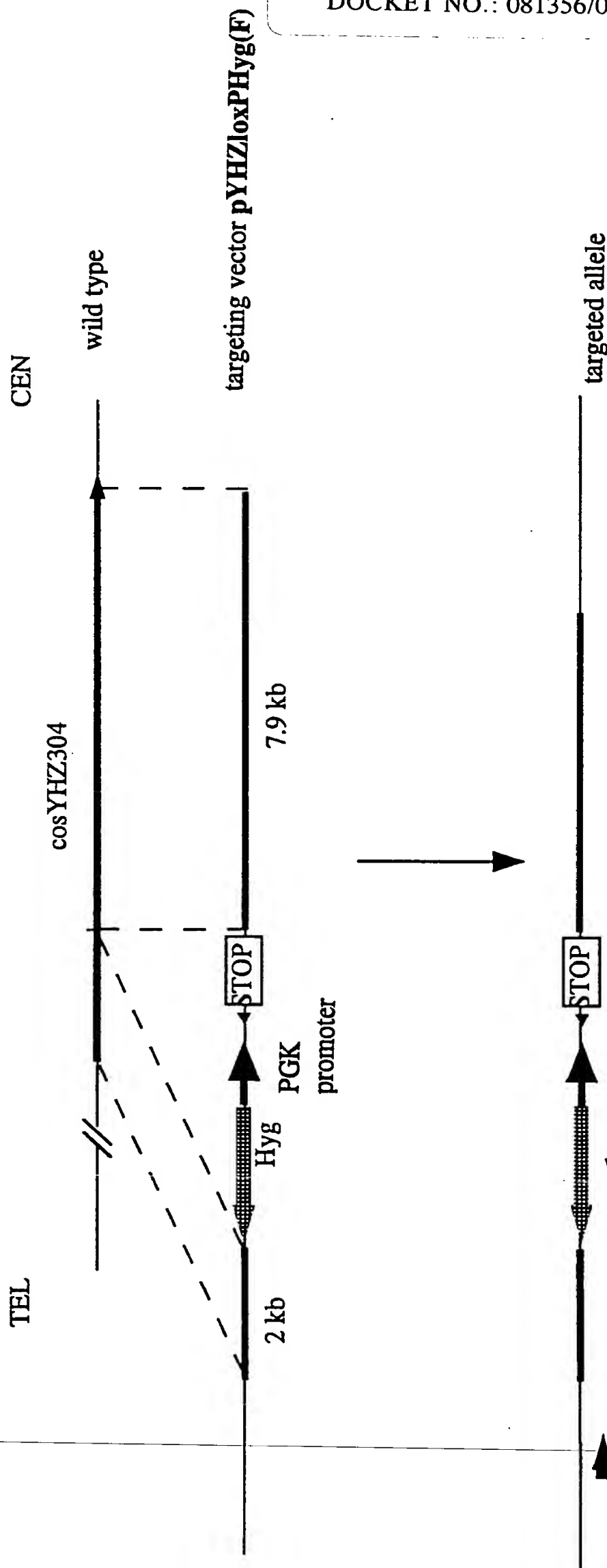
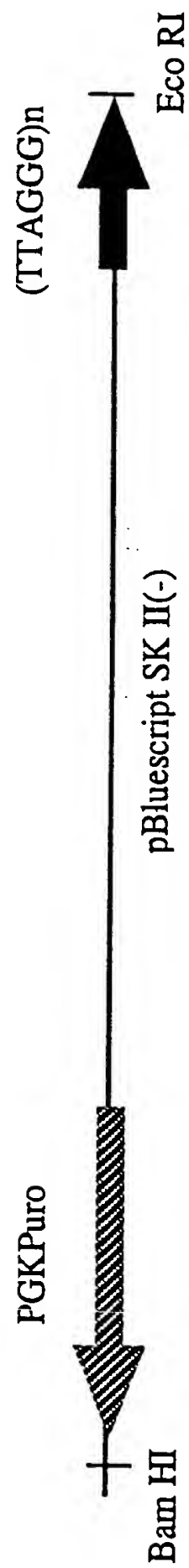


FIG. 64

FIG. 65



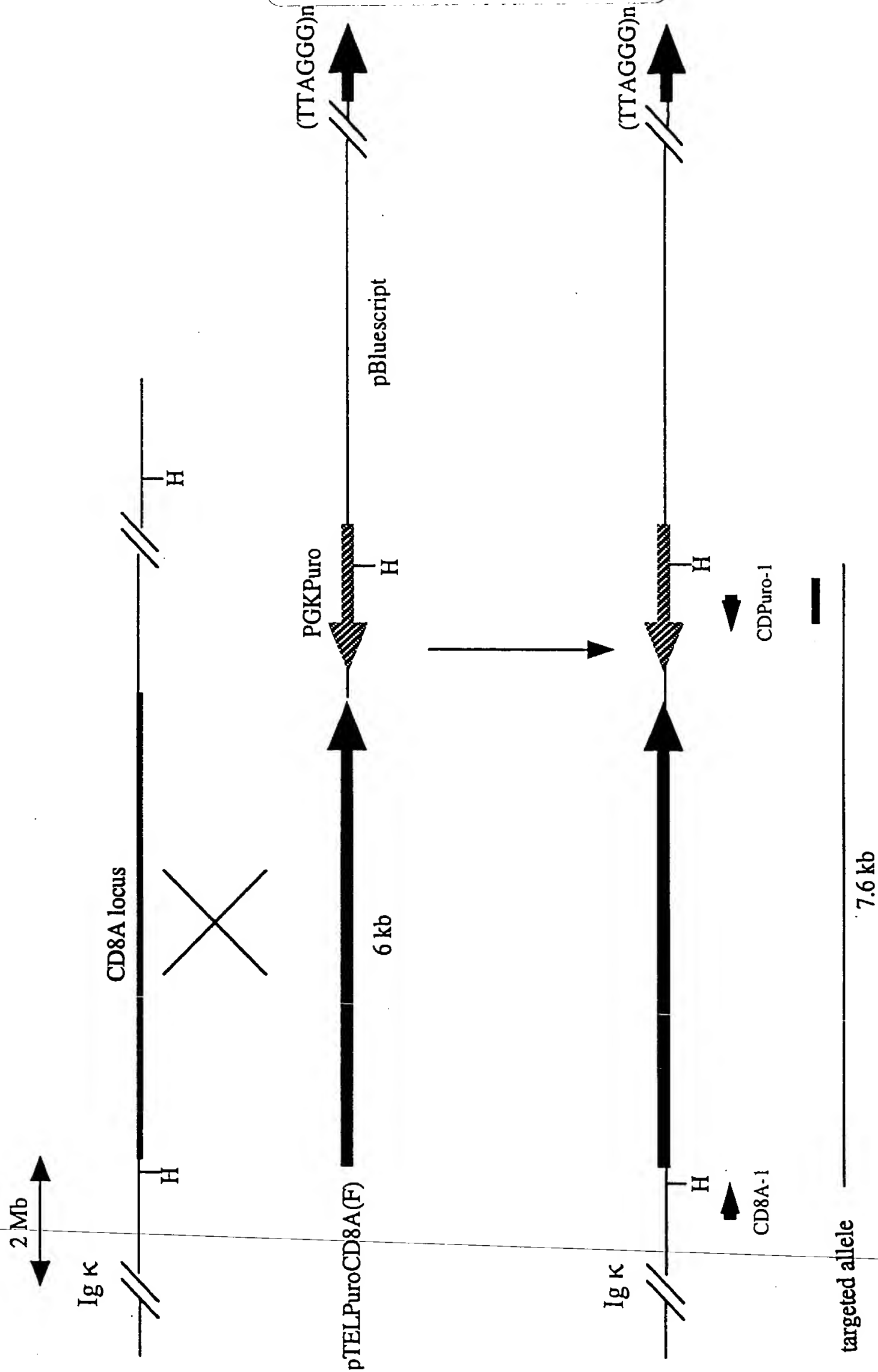


FIG. 66

09/763362

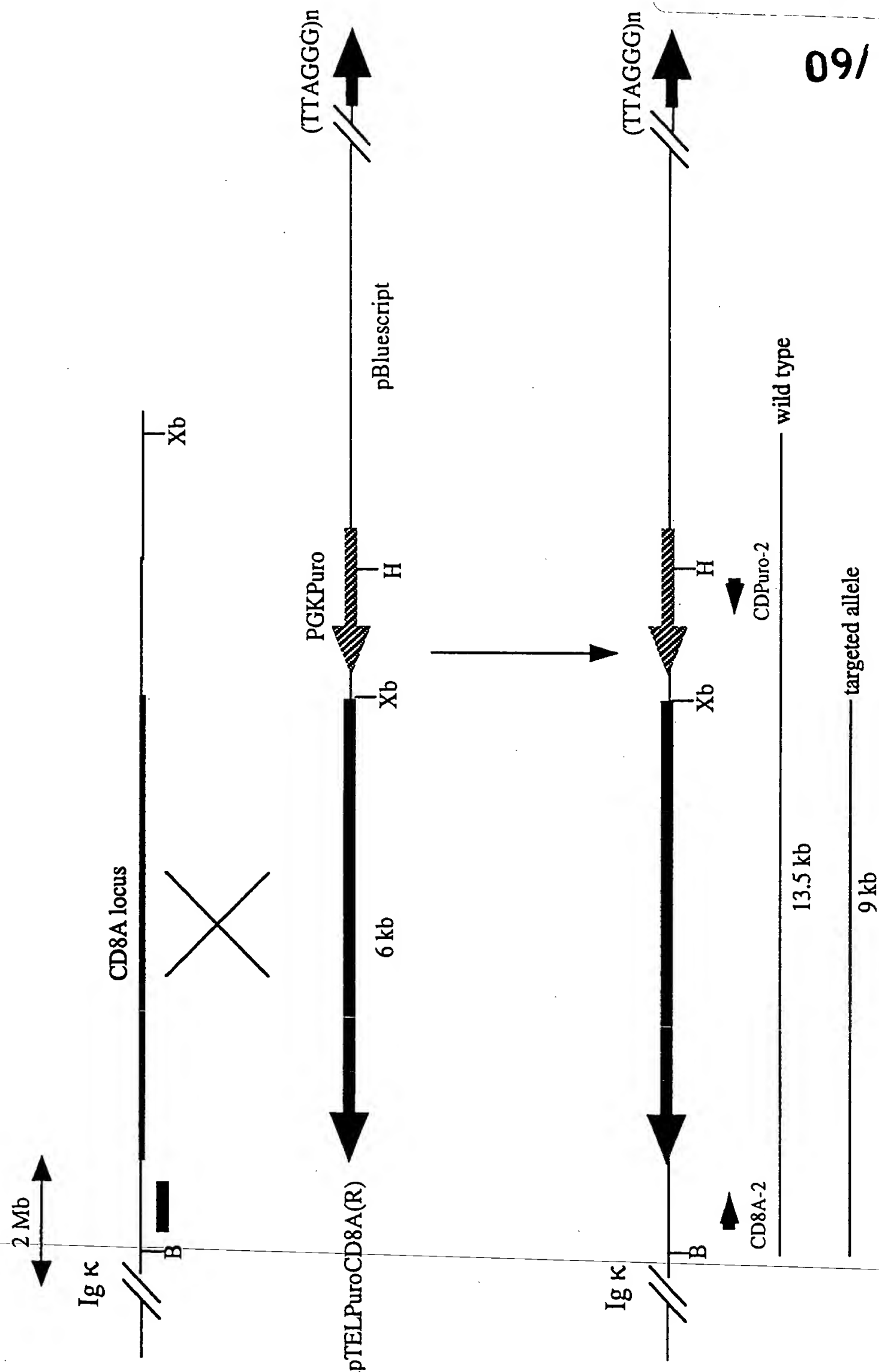
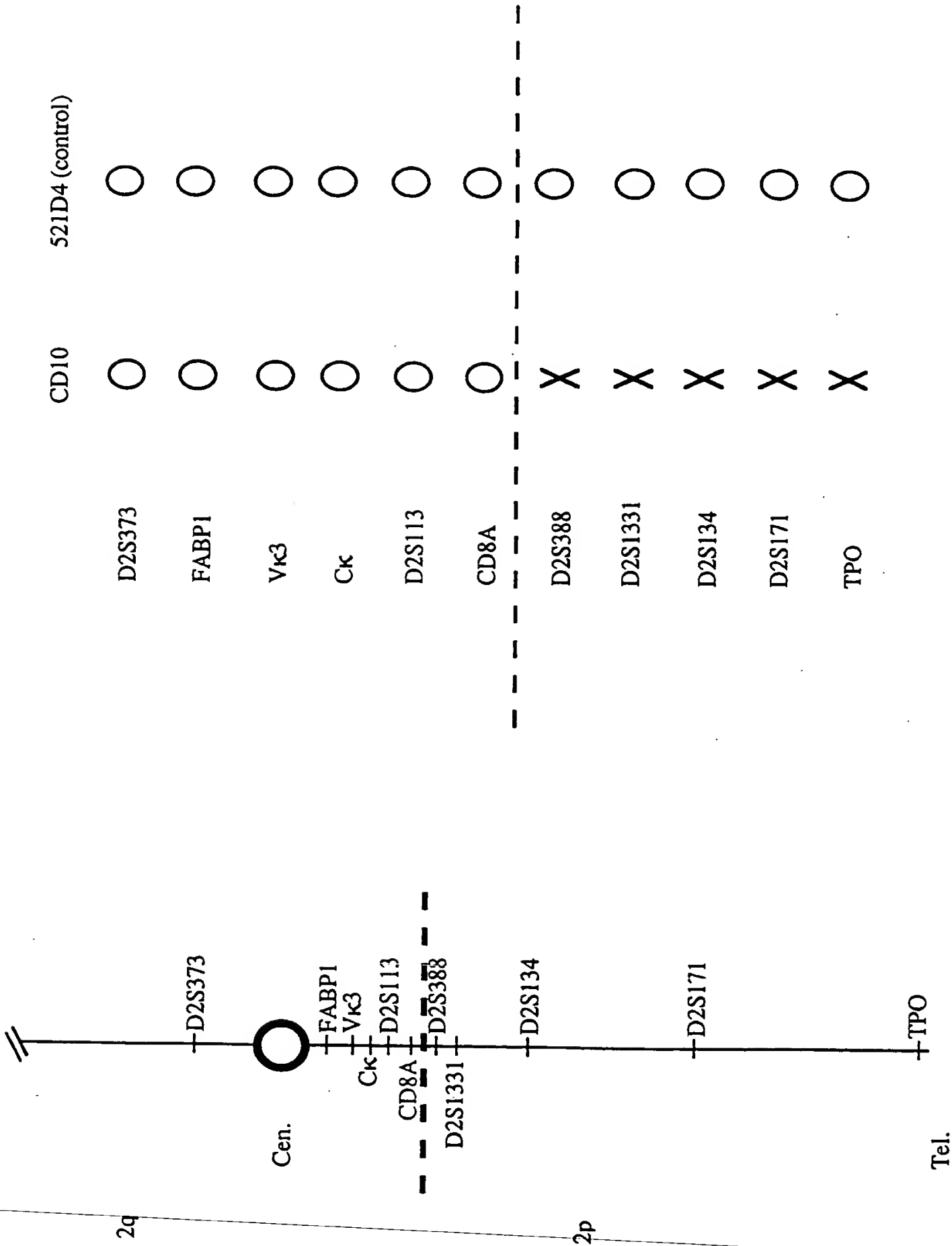


FIG. 67

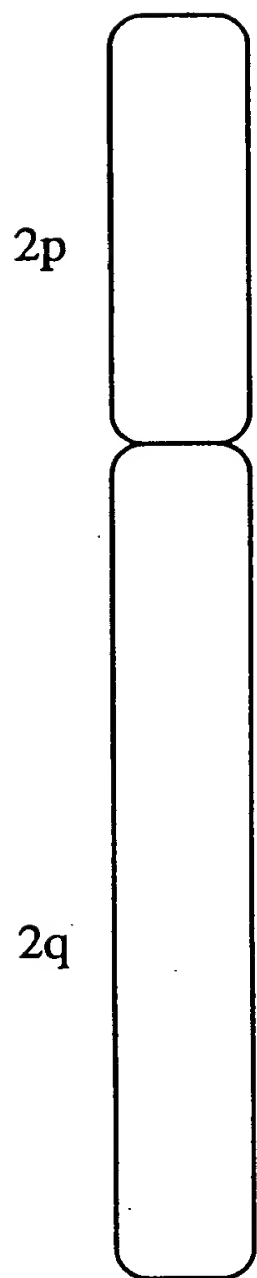
FIG. 68



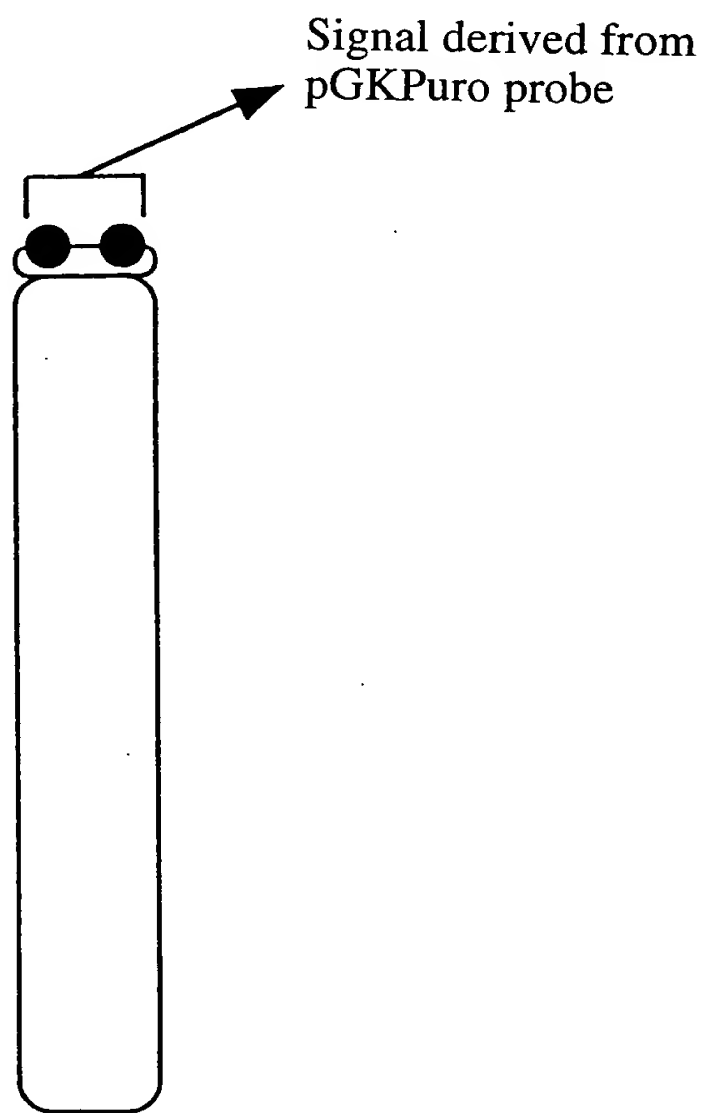
Human chromosome 2

FIG. 68

FIG. 69



521D4



CD10

FIG. 70

pBS185hisD

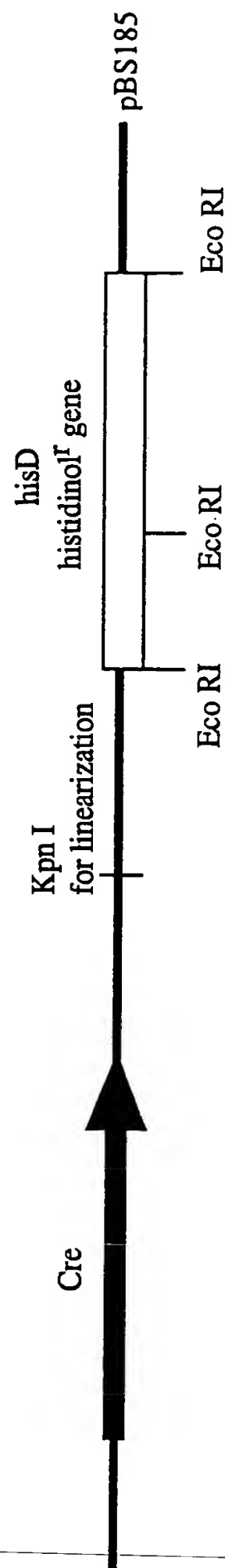
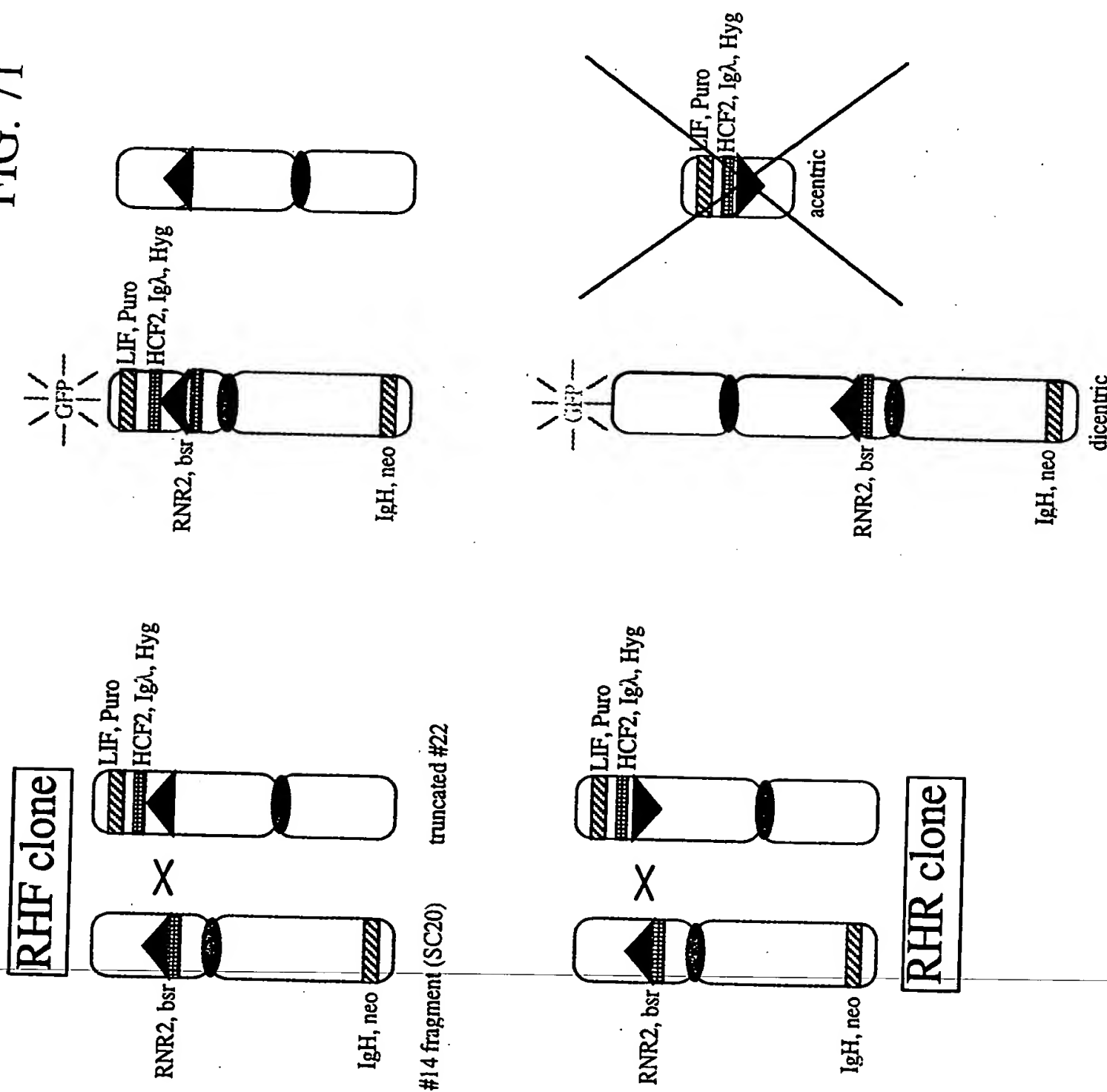


FIG. 71



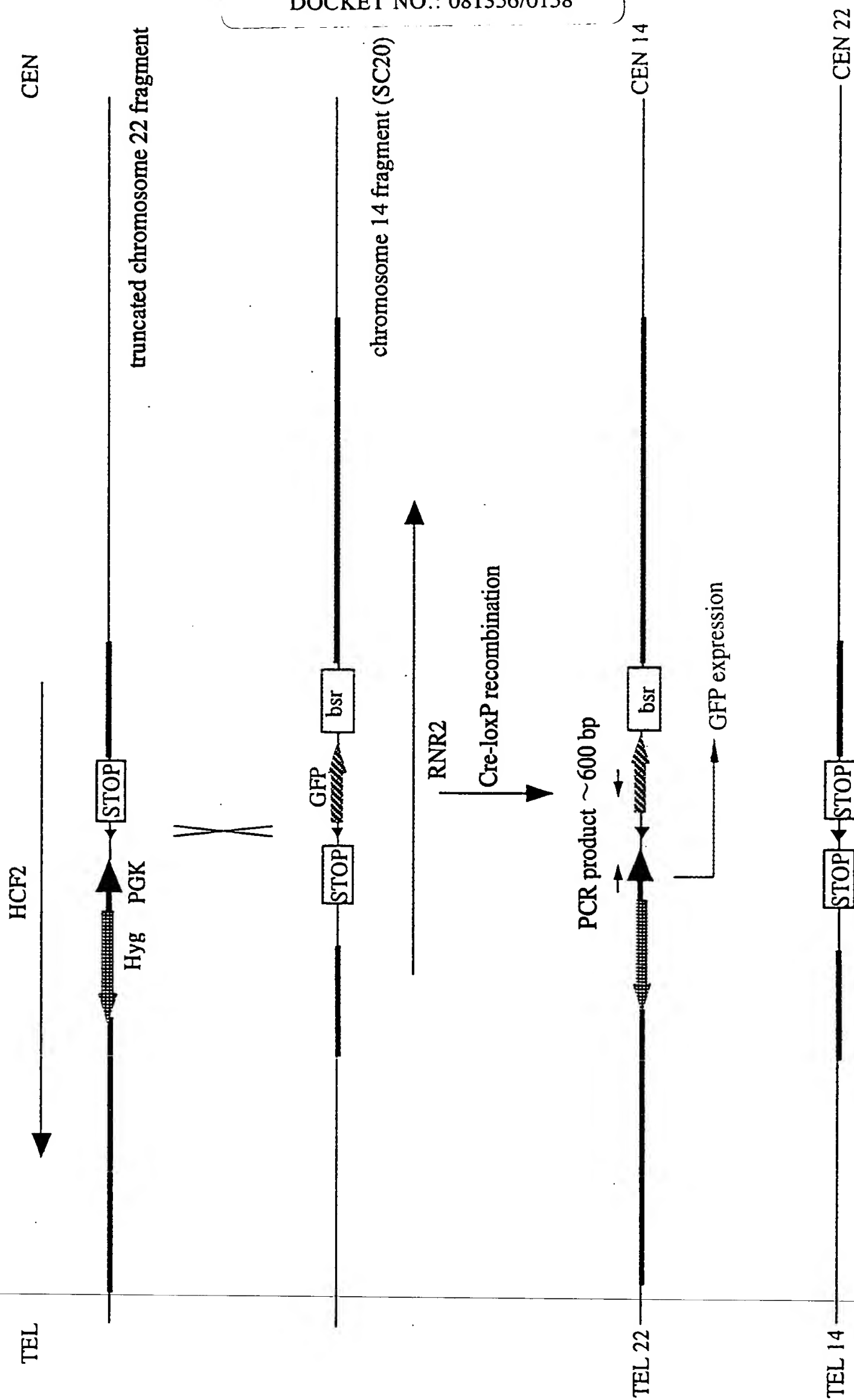


FIG. 72

FIG. 73



FIG. 74

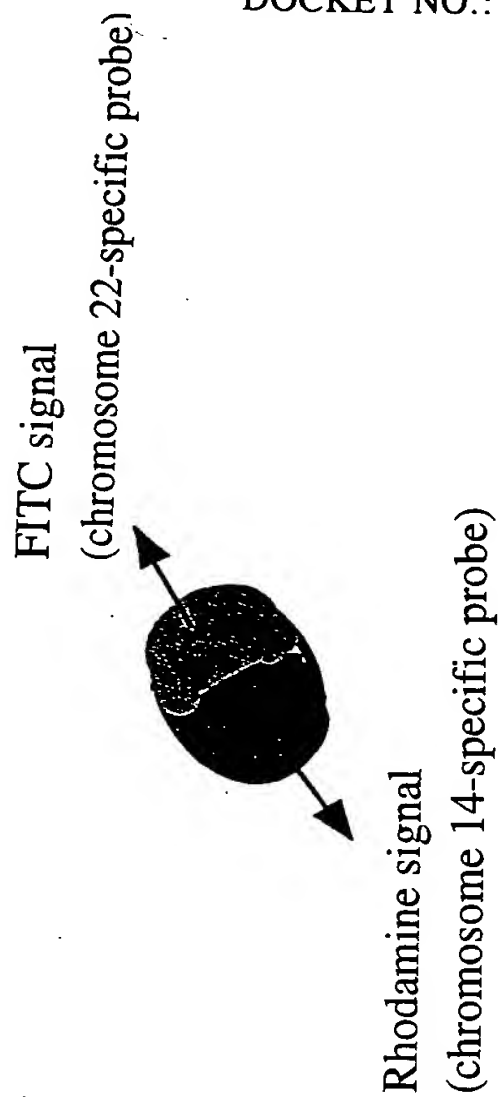
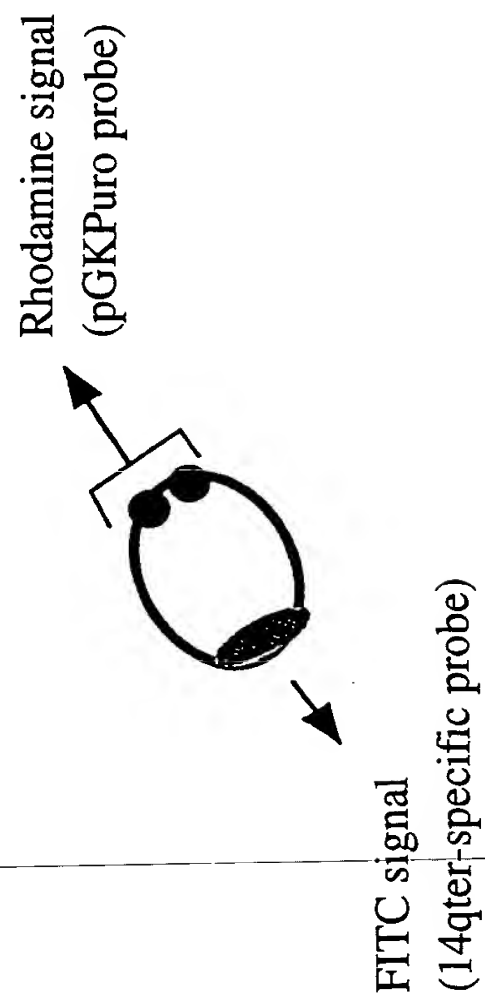


FIG. 75

